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CONTENTS OF PREVIOUS NUMBERS

NOVEMBER, 1919. NUMBER 5

Factors Determining the Relative Intensity of the Heart Sounds in Different Areas. An Experimental Study. Carl J. Wiggers, M.D., Cleveland.

Prolongation of the "S-T" Interval of the Ventricular Complex as Shown by the Electrocardiograph. Jonathan Meakins, M.D., Montreal, Can.

Progressive Lenticular Degeneration Associated with Cirrhosis of the Liver (Wilson's Disease). C. F. Howard, M.D., and C. E. Royce, M.D., Iowa City, Iowa.

The Energy Index (S.D.E. Index) of the Circulatory System. Joseph H. Barach, M.D., Pittsburgh.

Meningococcus Meningitis at Camp Lee. Russell L. Haden, M.D. (Detroit), Camp Lee, Va.

The Cholesterol Content of the Blood in Various Hepatic Conditions. M. A. Rothschild, M.D., and J. Felsen, M.D., New York.

Three Cases of "Renal Glycosuria." Frederick M. Allen, M.D., Mary B. Wishart and L. Millard Smith, Lakewood, N. J.

A Group of Sixty-Eight Cases of Type I Pneumonia Occurring in Thirty Days at Camp Upton. With Special Reference to Serum Treatment. Charles F. Tenney, M.D. (Toledo), and William T. Rivenburgh, M.D. (Highland, N. Y.), Camp Upton, N. Y.

The Determination of Hemoglobin by the Acid Hematin Method. Louis Berman, New York.

A Study of the Renal Concentration Power for the Uric Acid in Early Chronic Interstitial Nephritis. Preliminary Paper. Roy Upham, M.D., and Henry Allen Higley, M.D., Brooklyn.

Roentgenographic Studies in Gout. C. W. McClure, M.D., and E. D. McCarty, M.D., Boston.

DECEMBER, 1919. NUMBER 6

Botulism. A Study of the Resistance of the Spores of Bacillus Botulinus to Various Sterilizing Agencies Which Are Commonly Employed in the Canning of Fruits and Vegetables. Ernest C. Dickson, M.D., Georgina S. Burke, M.D., and Engelina S. Ward, A.M., San Francisco.

A Study of Pneumococcus Carriers. Joseph Sailer, M.D., Philadelphia; Milton W. Hall, M.D., Camp Jackson, S. C.; Robert L. Wilson, M.D., Jeannette, Pa., and Charles McCoy, M.D., M. C., U. S. Army.

The Basal Metabolism in Exophthalmic Goiter. J. H. Means, M.D., and J. C. Aub, M.D., Boston.

Antipyretics. I. The Benedict Respiration Chamber at the New Haven Hospital. Henry G. Barbour, M.D., New Haven, Conn.

Antipyretics. II. Acetylsalicylic Acid and Heat Regulation in Normal Individuals. Henry G. Barbour, M.D., and Michael M. Devenis, M.D., New Haven, Conn.

Antypyretics. III. Acetylsalicylic Acid and Heat Regulation in Fever Cases. Henry G. Barbour, M.D., New Haven, Conn.

Mental Disorders Following Influenza. Alfred Gordon, M.D., Philadelphia.

The Electrocardiogram and Ventricular Preponderance. Edward Perkins Carter, M.D., and Carl H. Greene, Ph.D., Baltimore.

The More Common Gases: Their Effect on the Respiratory Tract. Observation on Two Thousand Cases. Robert S. Berghoff, M.D., Chicago.

Index to Volume 24.

JANUARY, 1920. NUMBER 1

Harmful Effects of Shallow Breathing with Special Reference to Pneumonia. Jonathan Meakins, M.D., Montreal.

Contributions to the Physiology of the Stomach. LII. Studies on Gastric Ulcer. A. C. Ivy, Ph.D., Chicago.

The Effect of Roentgen Rays on the Metabolism of Cancer Patients. Richard N. DeNiord, M.D.; Bernard F. Schreiner, M.D., and Hollis H. DeNiord, M.D., Buffalo.

The Cerebrospinal Fluid in Multiple Sclerosis. Joseph Earle Moore, M.D., Baltimore.

Cavity Formation and Annular Pleural Shadows in Pulmonary Tuberculosis. James A. Honeij, M.D., New Haven, Conn.

Rat Bite Fever. Report of a Case. Aaron Arkin, A.M., M.D., Ph.D., Morgantown, W. Va.

The Protein and Lipin Content of Blood Serum in the Nephritides. Max Kahn, M.D., Ph.D., New York.

FEBRUARY, 1920. NUMBER 2

A Study of the Colloidal Gold Reaction and Its Clinical Interpretation. Margaret Warwick, M.D., and Charles E. Nixon, M.D., Minneapolis.

An Analysis of the Spread of the Excitation Wave in the Human Ventricle. George Fahr, M.D., Madison, Wis.

A Clinical Study of Yellow Fever. Observations Made in Guayaquil, Ecuador, in 1918. Charles A. Elliott, M.D., Chicago.

Pericarditis with Effusion. An Experimental Study. Charles Spencer Williamson, M.D., Chicago.

Book Reviews.

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Archives of Internal Medicine

Vol. 25 MARCH, 1920 No. 3

STUDIES ON ARTHRITIS IN THE ARMY, BASED ON FOUR HUNDRED CASES

I. PREAMBLE AND STATISTICAL ANALYSIS

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WITH THE ASSISTANCE OF
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The decision of the surgeon general to make special provision for the care and study of chronic arthritis in the Army, has permitted activities in this connection on a scale larger than has been possible in this country since the Civil War, or than seems likely to be possible again. The advisability of such provision was indicated by several factors. Statistics available through the courtesy of Col. A. G. Love, of the Sick and Wounded Division, U. S. Army, Washington, D. C., based on data available up to Jan. 1, 1918, indicated that for an army of four million men, for one year, there could be expected an incidence of upward of thirty thousand cases of chronic arthritis, excluding those of a tuberculous or a Neisserian nature. The very limited degree to which our troops had participated in active warfare at the time of compiling the above data suggested that with the subjection of more men to the same conditions these figures would be increased.

Observations by students of this subject among the Allied armies, and an independent survey of the cases presenting at a number of army hospitals in this country, gave added weight to these figures, not only in respect of the numbers, but also in respect of the types and severity of the cases encountered. It was plain, therefore, that chronic arthritis formed one of the larger medical problems affecting the soldier in service, and, hence, the efficiency of the army as a whole.

The marked chronicity of this disease, as compared with most outstanding medical conditions in the army, gives added importance to this fact. Further, the problem of the chronically arthritic soldier is extended to the civil community after his discharge in a degree which bears comparison with that of gunshot wounds. Finally, the incidence of chronic arthritis in civil life and the difficulty of meeting it are

already such as to make desirable efforts to prevent their increase and to justify any well considered action which seeks to utilize the large opportunities created by the war in the study of this disease.

Because of the fact that U. S. Army General Hospital No. 9, Lakewood, N. J., had already been designated as a center for investigative work; that it had a location easily accessible to returned overseas patients, and because of the presumably advantageous nature of the climate and soil there, the present studies were undertaken at this hospital.[1]

The lines of investigation followed were determined by several factors. Chief among these were the desirability of studying the metabolism of arthritis as a whole in a larger way than had yet been attempted by modern methods; the previous experiences of one of us (R. P.), which permitted a point of attack different from most lines of investigation, and the desirability of amplifying these experiences.

Most of the recent work undertaken on arthritis has proceeded from a bacteriologic basis, and this phase of the problem has been covered so thoroughly that it appeared improbable that much would be achieved in this direction without extraordinary effort; especially as the investigative personnel and equipment of the hospital were established along physicochemical lines. Bacteriologic studies in relation to chemical pathology were suggested, however, by the experience gained, and it is clear in retrospect that bacteriologic work of the nature indicated, would have been of interest.

The present report, therefore, considers the following: (a) the incidence of chronic arthritis in the army as a whole and a statistical analysis of the factors governing this incidence, the types of cases resulting and such clinical matters as have been suggested in the course of this study; (b) laboratory and clinical studies along a variety of lines, as to the nature of arthritis, based on a large number of the 400 cases presenting; (c) experiences with certain types of treatment, and a brief analysis of some other forms of therapy with their indications; (d) recommendations directed toward lowering the incidence of arthritis in the army, toward the provision of personnel, equipment and other facilities suggested by these studies as important, toward reduction of hospital days and toward the early return to duty of soldiers the subject of this disease.

This report does not aim to present the subject of arthritis in the form of a treatise. It attempts to reflect the conditions encountered,

1. The arthritic service was inaugurated at U. S. Army General Hospital No. 9, Nov. 16, 1918, and terminated with the closing of the hospital about June 1, 1919, although the admission of patients had ceased and the discharge of patients was completed about two weeks earlier.

to describe the work undertaken and to state such conclusions and recommendations as seemed warranted.

STATISTICS

Under average conditions, chronic arthritis has its highest incidence around the fourth and fifth decades, although it may occur at any age. The factors operating to produce it in young soldiers, under stress of warfare, presumably differ somewhat from those operating in civil life. It was conceivable that such differences might be reflected in a critical analysis of the cases presenting, and that other fact obtainable, such as the distribution of involvement, etc., would also be of interest. The study of each case began, therefore, with a critical and detailed examination as regards a considerable number of factors relating to the date and manner of the onset of the present attack; of the previous attacks, if any; the condition of health prior to the present attack; treatment received, and the like. A complete medical examination followed, including routine, full and differential blood counts, Wassermann test, etc., after which the subject was referred routinely for examination to the eye, ear, nose and throat department, the dental and genito-urinary departments and, when indicated, to the roentgen-ray department. Details regarding these examinations and the actions and conclusions based on them appear under the appropriate headings. Many of the patients were additionally made the subject of particular laboratory and other studies. Most of the patients in the present series were returned from overseas, although a considerable percentage came from camps in this country. More than 420 patients were admitted to or examined by the arthritic service, but the following statistics are based on 400 cases, after eliminating those of doubtful nature.

STATISTICAL ANALYSIS OF FOUR HUNDRED CASES OF ARTHRITIS ADMITTED TO U. S. ARMY GENERAL HOSPITAL NO. 9, LAKEWOOD, N. J.[2]

It was found that 256 patients (64 per cent.) had arthritis only; 112 (28 per cent.) had a combination of arthritis and myositis; twenty-two (5½ per cent.) had myositis only; seven (1.75 per cent.) had nerve involvement (neuritis) only, and three (0.75 per cent.) were listed as doubtful.

The average age of all patients was 28.26 years, while that of the worst cases showing the least improvement was 29.38 years.

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2. Compiled with the assistance of First Lieut. John W. Robertson, M. C. Associated at various times with the arthritis service at this hospital, were also Capt. Louis A. Levison, M. C., on whom fell much of the routine medical care of the patients, First Lieut. Willard Phippard, M. C., and First Lieut. Jacob Mitchell, M. C. It is a pleasure to acknowledge the cooperation of these officers, particularly Captain Levison.

The precipitating factors in order of frequency were as follows:

	No. Cases	Per Cent.
Exposure	232	58.
Dysentery	33	8.25
Injury	30	7.5
"Flu"	28	7.
"Gas"	23	5.75
Drilling and hiking	15	3.75
Tonsillitis	13	3.25
Pneumonia	6	1.5
Neisserian infection	4	1

Under a miscellaneous listing of precipitating factors:

1 case followed meningitis
2 cases followed appendicitis
2 cases followed measles
3 cases followed mumps
2 cases followed scarlet fever
1 case followed the injection of pneumococcic vaccine
1 case followed acute bronchitis
2 cases followed "boils"
2 cases followed abscess of the jaw (from tooth)

It was found that in forty-eight cases (12 per cent.) there was more than one precipitating factor; for instance, exposure and dysentery may have played an equally important rôle in one and the same case.

Fifty-six cases (14 per cent.) were listed as having an unknown precipitating factor.

One hundred and forty-three patients (35.75 per cent.) had had attacks of "rheumatism" prior to their army service. In contrast to this only eight of 113 nonarthritic patients (7 per cent. plus) on the surgical and orthopedic wards, questioned at random as to any history of "rheumatism," had had attacks of this nature. In other words, the incidence of previous attacks of arthritis or "rheumatism" was five times more frequent in the cases in this series than in cases at large admitted to the hospital for other conditions. This point is referred to more fully under the caption "Summary."

Statistics compiled under the direction of Capt. Bertnard Smith, chief of the cardiovascular department of the hospital, and made available through his courtesy, showed that in 350 cases of functional cardiac disorder, the incidence of rheumatic attacks prior to admission to the hospital was less than 6 per cent.

DISTRIBUTION OF INVOLVEMENT

	No. Cases	Per Cent.
Knee	248	62.
Ankle	141	35.25
Hip	135	33.75
Shoulder	127	31.75
Legs (muscle)	89	22.25
Hand	58	14.50
Spine	54	13.50
Foot	48	12.
Wrist	47	11.75
Elbow	39	9.75
Back (muscle)	33	8.25
Arm	30	7.50
Thigh	28	7.
Ileosacral joint	16	4.
Heel	7	1.75
Sciatic nerve	4	1.
Jaw	3	0.75
Lumbosacral joint	2	0.50
Facial nerve	1	0.25

It was noted that 228 cases (57 per cent.) showed a combination of two or more of the above distributions, ranging in a few cases up to involvement of practically all joints in the same case.

RELATIVE TO SURGICAL FOCI

The accepted relation of foci of infection to many cases of arthritis made desirable careful analysis of all cases in this regard. Fuller consideration of this analysis follows presentation of the figures resulting.

One hundred and seven persons (26.75 per cent.) were taken sick in the apparent absence of demonstrable surgical foci. Two hundred and ninety-three persons (73.25 per cent.) showed demonstrable surgical foci. Of this latter number 208 showed foci in the tonsils. This is 52 per cent. of the entire series and is 71 per cent. (minus) of all cases (293) showing foci.

One hundred and thirty-four persons (33.50 per cent.) in the entire series, or 45.73 per cent. of those showing a demonstrable surgical focus, were positive for a dental focus. Fifty persons, 12.50 per cent. in the entire series, or 17 per cent. (plus) of those showing a focus, were positive for a genito-urinary focus. Of the above 293 persons showing a focus in any of the above three distributions, seventy-eight (19.50 per cent. of 400) showed a combination of both dental and tonsillar foci. This is 26.62 per cent. of the 293 persons having a focus somewhere.

It was also found that thirty-eight persons showed some combination of foci other than dental and tonsillar, as for instance dental and genito-urinary or tonsillar and genito-urinary. This number was 9.50 per cent. of the entire series or 13 per cent. (minus) of the 293 persons showing foci.

Regarding Progress

No. Cases	Per Cent.	Remarks
92	23.	Recovered in the apparent absence of a demonstrable focus.
184	46.	Recovered in the presence of a demonstrable focus.
34	8.5	Recovered after the removal of foci.
31	7.75	Were improved after the removal of foci.
28	7.	Were unimproved after the removal of foci.
310	77.5	Recovered "by whatever means."
74	18.5	Improved "by whatever means."
16	4.	Were unimproved "by whatever means."

On a basis of the last 100 cases of the series, investigated more fully for this point, five patients (5 per cent.) improved in the apparent absence of foci; twenty-five (25 per cent.) improved in the presence of unremoved foci.

Several points of interest are developed from a study of these figures. Exposure took precedent of all other factors as the exciting agent. There is, of course, in any statistical compilation room for error in the emphasis placed on any one factor, but the clear-cut statements of the soldiers questioned, and the unanimity with which these agreed, made it clear that after making all allowances for error, exposure to cold and wet is a factor of major importance in producing rheumatoid and arthritic disabilities among soldiers in service under present conditions of warfare.

By the term "exposed to cold and wet" is meant protracted subjection to such conditions as deep mud or heavy rain which kept the men, or at least their legs and feet and often their entire bodies, wet for hours, days or even weeks at a stretch. Sleeping consecutive nights on stone or cement floors or wet earth in stone outhouses is also included under this head, and figured frequently not only in the histories elicited, but as causative factors in the conscious experiences of the men themselves. In one extreme example of this series, disability dated abruptly from being caught between allied and enemy fire in a swamp where the command was forced to remain sixty hours, during which time this soldier was in water up to his knees. Other such and repeated instances leave no doubt as to the etiologic relation of exposure of various kinds.

It is of interest that the factor next most frequently encountered after a marked percentage drop was dysentery, which is separated by relatively small differences from injury and "flu." Under "Clinical Considerations," mention will be made of certain points of interest in this connection. It is noteworthy that drilling and hiking were recorded as the exciting factors in only a small percentage of cases, namely, 3.75 per cent.

Analysis of the distribution of involvement indicates that the frequency of disability in the knee is outstanding in contrast to involve-

ment of the ankle, hip and shoulder. This suggests an immediate influence from trauma on the weight bearing parts. The frequency, however, of involvement of the knee under civil conditions, the fact that the shoulders were involved almost as frequently as the hip and ankle; the fact that in a great majority of instances the disease was more or less systemic in its manifestations, and the impressive evidence adduced by the men themselves in relating their disabilities to cold and wet, would seem to indicate that mechanical agencies, such as trauma in marching, played a rôle not conspicuously greater than they do in civil life.[3]

The involvement of the jaw among soldiers was conspicuously infrequent as compared with civil life. The phalangeal and metacarpophalangeal joints of the hand were involved in 14½ per cent.

Certain interesting and instructive relations were indicated by the analysis of all cases presenting in this series for surgical foci in any part of the body. As mentioned, efforts to this end formed one of the fundamental bases of study and treatment of this group.[4] It is generally conceded that the most frequent sites of focal infection are the tonsils, teeth, genito-urinary tract and accessory sinuses of the head, although it may occur almost anywhere in the body. The question of what constitutes pathology, particularly in the tonsils, and when it potentially operates as a focus of infection is a matter on which there is much room for discussion, and it is probable that no observations to this end can be immune from criticism. It is particularly difficult to determine the absence of all foci of infection, and in this connection evidence must be largely presumptive, however carefully obtained. Studies at the hands of many observers, and experience afforded by the work here presented, indicate that harmful foci may be contained within tonsils deeply buried and innocuous in appearance. At the hands of critical observers, however, it is possible to indicate, in a great majority of cases, when present, the existence of definite pathology, particularly perhaps in the teeth, where the roentgen rays often confirm or refute suspicious evidence. It is probable, therefore, that the error on the positive site is small.

Referring to the figures, it will be noted that 107 patients, or about 27 per cent., were taken sick in the apparent absence of demonstrable surgical foci in the head, nose, throat, teeth or genito-urinary tract.

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3. In a thorough analysis of the results of tonsillectomy in 200 consecutive cases of myositis and arthritis, Lillie and Lyons (J. A. M. A. **72**:1214 [April 26] 1919) found that under civil conditions the knees were involved with greater frequency than other joints.

4. Obligation is expressed for the painstaking and cooperative efforts of the medical officers conducting the department of the eye, ear, nose and throat; especially Capt. Watson W. Gailey, Jr., and Capt. T. W. Davis, M. C., U. S. Army.

Bearing in mind that there is a possible error in the exact number classed in this category, it nevertheless becomes apparent that an important percentage of these soldiers were free from the gross pathology so frequently found in civil life in connection with this disease. On the other hand, 184 patients, or 46 per cent., recovered in the presence of demonstrable foci. This fact is particularly instructive. It is less impressive when indicated by figures than when demonstrated by intimate contact with scores of men, invalided for months, and, in many cases, a year or more by severe and widespread arthritis, who have achieved recovery without residual pathology along lines of expectant treatment, aided sometimes by local measures. Under the pressure of war conditions, it was clearly difficult or impossible to give these men the attention they deserved and should have had. In view of the large rôle played by exposure as an exciting factor; in view of the recovery from arthritis of many soldiers carrying demonstrable surgical foci, usually in their tonsils, it is impossible to escape the conclusion that the men constituting the group here studied, showed a large independence of focal infection. It is to be borne in mind that many men were convalescing or well on admission to the hospital. Many men would certainly have gotten well sooner had their foci been removed. It should not be deduced that the removal of foci is unimportant. It is of great importance and is made the basis of one of the recommendations to be mentioned later. In this particular group, however, it must be recognized that more men got well with no attention to foci than got well after removal of them. This conclusion will appear somewhat at variance with the relation focal infections are known frequently to bear to the disease, and should not be interpreted as justifying neglect of this established rôle; indeed, the evidence adduced from this series substantiates this relation strongly. Bearing this relation in mind, however, it is proper, if possible, to establish its limits etiologically and therapeutically. It is probable that there is here evidenced a distinct contrast to the conditions influencing chronic arthritis in civil life, and that the age of the subjects and the recuperative powers of youth must be given large significance. Under "Treatment," mention will be made of the possible practical application of this conclusion.

It is of much interest to note that only fifty cases, or 12½ per cent., of the series showed a possible focus in the genito-urinary tract. Indeed, of this number showing demonstrable pathology, only a trifling number were believed to have actual relation to the intercurrent arthritis, and it seems safe to conclude that genito-urinary infections played a small rôle in the causation of chronic arthritis in the army. The focal genito-urinary infections found were referable in only a

small percentage to venereal disease per se.[5] It is also of interest to note that only eight cases, or 2 per cent., showed a sustained and undoubtd Wassermann reaction. This entirely corroborates the experience of one of us (R. P.) in civil life, and there seems little doubt that syphilis plays a negligible rôle in the causation of chronic arthritis.

DENTAL FOCI

An analysis of 397 cases for the percentage incidence of the various types of dental pathology was prepared by Capt. W. E. Mentzer, Dental Corps, to whom obligation must be expressed for cordial and skilful cooperation.[6] As noted above, definite dental foci of infection presented in only 134 cases, or 33½ per cent., and tonsillar foci were present in 208 cases, or 52 per cent. It is rather astonishing that the combination of tonsillar and dental pathology should be present in only seventy-eight, or 19½ per cent. of the entire 400 cases. This was not due to over-attention to one focus, when found, with consequent neglect of other possible foci, as all cases were examined routinely and independently.

In examining patients from the dental standpoint, any condition about the mouth from which absorption might take place, was considered a possible focus, and the case was studied further from that standpoint. The subject of caries was divided into three classes, respectively, slight, medium and heavy, to assist the dental department in giving attention first to the most needy cases. Under "caries slight," are classed the cases in which the enamel was etched or just broken; under "caries medium," are classed the cases in which the decay had proceeded farther, but not far enough to endanger the pulp, and under "caries heavy," are classed the cases in which the pulp was endangered or already exposed.

Conditions falling under the classifications "simple gingivitis," and "condition of the gums, fair or poor," were not regarded as foci, but were considered as paving the way for infection and suppuration, and were corrected immediately to prevent the deeper tissues from becoming involved. The number of cases falling under "gingivitis simple," and "condition of gums poor," was large owing to the fact that these patients were not able to give their mouths the average amount of care. This is illustrated by the number of subjects showing salivary deposits. Under "pockets" about the necks of teeth have been listed all cases where such conditions were found, whether suppurative or

5. Opinion of Capt. George G. Smith, chief of the genito-urinary service at U. S. Army General Hospital No. 9.

6. All 400 cases were analyzed for dental foci as mentioned, but calculation of the percentage incidence of different kinds of dental pathology was made on only 397 cases.

nonsuppurative. Very few of these cases were suppurative; the larger number, being caused by calculus deposits or the impaction of food between the teeth, had not progressed to that degree. When ulcerative gingivitis was present, or when there were pockets about the necks of the teeth, it became necessary for the examiner to determine whether in his opinion the condition present constituted a focus or not.

Under abscessed teeth come the various alveolar abscesses, acute, chronic (with and without sinus) and blind abscesses, all of which were classed as constituting foci. The roentgen rays were resorted to when there were deep pockets about the necks of the teeth and in all cases in which there was the least possibility of an apical abscess. An analysis of 397 cases revealed the following conditions in the proportions indicated.

Caries, slight ..... 118; not constituting a focus
Caries, medium ..... 80; not constituting a focus
Caries, heavy ..... 79; not constituting a focus
Calculus, subgingival ..... 211; not constituting a focus
Calculus, salivary ..... 116; not constituting a focus
Condition of gums, good..... 164; not constituting a focus
Condition of gums, fair..... 103; not constituting a focus
Condition of gums, poor..... 112; not constituting a focus
Gingivitis, simple ..... 216; not constituting a focus
Gingivitis, ulcerative, 25, constituting a possible focus;
Pockets about necks of teeth, 77, constituting possible foci;
Abscessed teeth, 126, constituting foci of infection; Incidence of abscessed teeth among all cases examined, 30 per cent.

Only nine cases showing either pockets about the necks of the teeth or ulcerative gingivitis, or both, were considered actual foci of infection, making a total of 135 instances, or 34 per cent.

STUDIES ON ARTHRITIS IN THE ARMY BASED ON FOUR HUNDRED CASES

II. OBSERVATIONS ON THE BASAL METABOLISM

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Few, if any, observations have been available to date on the basal metabolism of chronic arthritis. Some of the evidence regarding this disease has indicated that a variety of agents whose action is supposed to hasten the body metabolism, such as thyroid extract, radium and the roentgen ray, may, at times, exercise definitely beneficial effects, and that certain subjects of chronic arthritis do very much better on a lowered food intake, particularly of carbohydrate, than they do on an unrestricted diet.[1] These, and other, considerations have suggested that there might be in chronic arthritis a lowering or retardation of the body metabolism which would express itself in summation figures; although it is, of course, possible that the intermediary metabolism might be markedly disturbed without being reflected in such totals. The basal metabolism was, therefore, studied in a series of twenty-nine cases. The observations were made by indirect calorimetry, using the Tissot method. Analyses of the expired air were carried out on the Haldane gas apparatus.[2] Table 1 shows the results obtained. Of the twenty-nine cases studied, 80 per cent. showed a metabolism within normal limits; 20 per cent. showed a metabolism slightly below normal limits.[3] The metabolic data give no explanation for this deviation. From the respiratory quotients no abnormality can be detected in the percentage of calories obtained from the three foodstuffs. Nothing abnormal was found in the pulse, temperature or minute volumes of air breathed at the times of the determinations. In the cases showing a basal metabolism below the normal limits, no particular relation could be determined between the severity of the disease, age or condition of the patient (whether active or bed-ridden), atrophy of muscle, edema or other factors.

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1. Pemberton, R.: Am. J. M. Sc. **153**:678 (May) 1917.
2. Peabody, Wearn and Tompkins: The Basal Metabolism in Cases of the Irritable Heart of Soldiers, Med. Clin. N. America **2**:507 (Sept.) 1918.
3. The second experiment on Robbins is not included in either percentage because he was then on a limited diet.

TABLE 1.—Basal Metabolism in Twenty-Nine Cases of Chronic Arthritis

Name	Case	Date	Age	Height, Cm.	Weight, Kg.	Buccal Temperature F.	Pulse	C.c. of CO_2 per Minute	C.c. Oxygen per Minute	Respiratory Quotient	Volume per Minute, L.	Calories per Sq. Meter	Metabolism Percentage from Normal
Masood	10	11/21	23	167	57.7	98.8	75	186	226	0.83	5.13	39.8	—1
Grondyke	83	1/21	50	160	50.0	98.4	85	150	176	0.85	4.66	34.2	—2*
Brice	16	1/16	46	173	53.9	98.2	78	168	212	0.79	4.98	37.3	—3
Dekim	84	9/21	42	174	64.3	98.4	64	171	235	0.73	4.67	37.6	—3†
Leeman	85	9/22	19	174	58.2	97.8	67	219	227	0.97	6.55	40.0	—3
Hinman	11	12/13	25	161	57.0	97.5	52	181	206	0.88	4.91	38.1	—4
Stone	28	1/ 6	40	167	53.9	97.7	59	186	194	0.96	5.06	36.5	—5*
Cox	79	12/ 7	36	177	65.9	97.4	59	191	236	0.81	6.04	37.4	—6
Jaffy	7	11/22	24	168	50.7	98.2	73	156	208	0.77	4.70	37.1	—6
Hayes	6	12/ 7	29	180	56.6	97.7	68	167	218	0.77	4.51	36.2	—8
Robbins	1	11/19	25	192	78.4	98.7	69	229	257	0.89	5.90	36.6	—8
Robbins	1	1/ 6	..	...	77.3	97.6	61	184	245	0.75	4.86	34.2	—14
Lumers	13	1/ 9	40	163	47.3	97.0	67	134	169	0.79	3.83	22.8	—9
Beck	5	11/19	26	189	65.0	97.4	55	199	232	0.86	4.82	35.9	—10
Lowe	14	1/28	42	177	60.1	97.6	60	184	216	0.86	5.50	34.1	—11
Zuch	86	12/ 6	25	172	70.5	98.0	54	167	226	0.74	4.60	35.0	—12
Sharpe	87	12/ 4	46	178	78.4	97.8	62	191	229	0.84	4.64	33.8	—13
Haeberle	2	12/ 7	29	175	68.4	97.6	73	158	216	0.73	5.91	33.4	—15*
Blowers	3	12/ 2	41	179	68.2	97.7	58	169	211	0.80	4.89	32.7	—16
Martin	8	11/29	45	172	66.6	98.2	72	139	191	0.73	5.01	30.6	—21
Oberg	22	2/ 3	24	169	49.7	98.4	93	168	214	0.79	4.42	39.6	±0
Bartkiavicus	88	12/10	26	178	81.8	97.4	65	223	277	0.81	6.24	40.0	+1
Cichon	89	12/ 9	22	163	61.6	98.1	59	188	229	0.82	5.99	39.9	+1*
Mulledy	90	11/21	21	178	78.3	98.4	66	220	279	0.79	5.99	40.7	+3*
Saxton	91	9/22	24	181	71.6	98.0	65	207	270	0.77	6.04	40.5	+3
Kolden	92	9/21	28	171	60.7	98.0	72	205	251	0.82	5.71	42.2	+7‡
Hamburg	93	12/ 9	23	168	62.0	98.4	76	200	260	0.77	5.13	43.1	+9
Meadows	94	11/21	22	168	52.5	97.8	52	200	235	0.85	6.52	43.1	+9§
Boyd	12	12/13	24	165	49.5	98.5	80	199	228	0 87	5.45	43.7	+11

* Periods disagreed by 4 per cent.
† Periods disagreed by 5 per cent.
‡ Periods disagreed by 6 per cent.
§ Restless in Period II; periods disagreed by 8 per cent.

STUDIES ON ARTHRITIS IN THE ARMY BASED ON FOUR HUNDRED CASES

III. STUDIES ON THE NITROGEN, UREA, CARBON DIOXID COMBINING POWER, CALCIUM, TOTAL FAT AND CHOLESTEROL OF THE FASTING BLOOD, RENAL FUNCTION, BLOOD SUGAR AND SUGAR TOLERANCE

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NITROGEN AND UREA OF THE BLOOD

In previous communications[1] evidence was advanced to show that there is no disturbance of the fasting level of the blood urea or nonprotein nitrogen in cases of chronic arthritis. It was believed important, however, in studying the present relatively large group to include consideration of these factors in order further to substantiate or disprove these findings. Accordingly, determinations of blood nitrogen and urea were conducted in a series of seventeen cases. The blood samples were collected in the morning before the patient received his breakfast. Nonprotein nitrogen was determined by the direct nesslerization method of Folin and Denis[2] and blood urea by the method of Van Slyke and Cullen.[3] The figures herewith appended show that all cases, including those of the most severe type, fall well within normal limits. These observations were further supported by independent determination by Lieut. Thomas E. Buckman, M.C., on the blood nitrogen made in connection with studies on creatin and creatinin (see section devoted to this subject) using ten patients of the present series as well as many other patients, a total of fifty. In a series then of sixty-seven observations in fifty-seven cases of chronic arthritis the fasting blood nitrogen fell within normal limits in all but two cases. One of these patients was a man, aged 46 years, with cirrhosis of the liver and renal calculus, who gave 45.4 mg. of nitrogen per hundred c.c. of blood. The other patient was a man, aged 21 years, with a chronic arthritis of one knee, who gave 38.5 mg. There was no other evident disturbance of his health.

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1. Pemberton, R.: Am. J. M. Sc. **147**:423 (March) 1914.
2. Folin and Denis: J. Biol. Chem. **26**:473, 1916.
3. Van Slyke and Cullen: J. Biol. Chem. **19**:211, 1914.

TABLE 1.—Blood Urea and Nonprotein Nitrogen *

Name	Case	Date	Nonprotein Nitrogen, Mg.	Urea Nitrogen, Mg.
Heaberle	2	1/22	29.7	13.6
Robbins	1	1/ 9	30.5	14.2
Hayes	6	1/10-2/6	23.5	12.6
Martin	8	12/26	27.5	13.1
Jaffy	7	1/10	28.0	13.4
McGrann	4	1/10	28.2	18.2
Studebaker	15	1/16	29.3	15.0
Boyd	12	1/ 9	24.6	11.8
Hinman	11	1/ 6	....	14.5
Masood	10	12/31	....	14.0
Lowe	14	1/13	23.5	11.0
Wasson	20	1/29	30.0	14.0
Whittington	21	1/31	27.8	14.7
Oberg	22	1/31	23.0	11.2
O'Brien	23	2/ 4	26.3	10.4
Faulkner	17	1/22	22.3	11.0
Mrs. K.	53	3/29	25.0	11.3

* For further observations on nitrogen of the fasting blood, see the section on creatin, Part IV.

CARBON DIOXID COMBINING POWER OF THE BLOOD

Studies were conducted in a series of seventeen cases of chronic arthritis in respect of the carbon dioxid combining power of the blood as an index of acidosis. In three of these cases determinations were repeated, making twenty observations in all. In every case the figures fell well within normal limits, the lowest being 53 and the highest 67. The determinations were made on the blood plasma by Van Slyke's gastometric method.[4] Cases 6, 8, 7, 4, 10, 14 and 22 of this series showed advanced disease.

TABLE 2.—Plasma Bicarbonate

Name	Case	Date	CO_2 Volume per Cent.	Date	CO_2 Volume per Cent.	Remarks
Haeberle	2	1/22	64	...	..	Great bone atrophy
Robbins	1	12/30	64	...	..	Severe type
Hayes	6	12/26	57	...	..	Severe type
Martin	8	12/26	65	...	..	Severe type
Beeman	9	12/26	64	...	..	Mild type
Jaffy	7	1/10	58	...	..	Severe type
McGrann	4	1/10	54	...	..	Quite severe
Studebaker	15	1/16	64	...	..	Quite severe
Boyd	12	1/ 9	65	...	..	Intermittent type
Hinman	11	1/ 2	69	1/6	62	Mild type
Masood	10	12/31	61	1/2	59	Severe type
Lowe	14	1/13	58	...	..	Severe type
Wasson	20	1/29	67	...	..	Severe type
Whittington	21	1/31	67	...	..	Quite severe
Oberg	22	1/31	59	2/4	67	Severe type
O'Brien	23	2/ 4	58	...	..	Severe type
Faulkner	17	1/22	61	...	..	Mild type

4. Van Slyke: J. Biol. Chem. **30**:397, 1917.

THE CALCIUM OF THE CIRCULATING BLOOD

In view of the known absorption and deposition of lime salts in chronic arthritis affecting the osseous tissues, it was thought interesting to include observations on the calcium in the fasting blood in various types. There can be little question that in the processes which result in atrophy or overgrowth of bone there is a disturbance of the normal calcium balance between the fixed and the fluid tissues and possibly of the total body balance as well. Goldthwaite, Painter and Osgood[5] have reported a loss of calcium in the cases of atrophic and hypertrophic arthritis studied by them. It was not practicable, however, to conduct calcium balance determinations in the present series. Clinically, cases and types of arthritis differ markedly in respect of the absorption or deposition of bony tissue, and dependable variations of the blood calcium might be of value for differential diagnosis or classification. Observations were accordingly made on the blood calcium under fasting conditions by means of Lyman's nephelometric method.[6] Ten cases were studied, and the results obtained were found to fall with surprising uniformity within normal limits, corresponding well with other determinations made in the same laboratory on other types of disease and on healthy individuals. The cases studied were mostly of great severity, although three patients of the series represented milder types.

TABLE 3.—BLOOD CALCIUM

Name	Case	Date	Calcium, Mg. per 100 C.c.	Remarks
Lowe	14	4/ 8	7.1	Severe
Jaffy	7	4/ 8	7.3	Convalescing
McIntyre	09	4/ 8	7.3	Moderate
Hayes	6	4/ 8	7.2	Severe
Whittington	21	4/ 9	6.5	Moderate
Crawford	71	4/ 9	7.2	Severe
McKensie	02	4/28	7.3	Severe, intermittent
Oberg	22	4/28	7.2	Severe
Cotter	55	5/ 1	7.3	Mild
Jansen	48	5/ 3	7.1	Improving

THE TOTAL FAT AND CHOLESTEROL OF THE FASTING BLOOD

A considerable field of investigation has been opened up of late in connection with the blood fats and cholesterol and their relation to metabolism; more particularly since the introduction of Bloor's simpler analytical methods. There has been made possible the accumulation of data in a variety of pathologic conditions tending to place certain

5. Goldthwaite, Painter and Osgood: Am. Med. **7**:547, 590 (April 2 and 9) 1904.

6. Lyman: J. Biol. Chem. **29**:169, 1917.

phases of the metabolism of fat on a basis analogous to that obtaining with the nitrogen and urea of the blood. Apart from the desirability, on general grounds, of utilizing these methods in studying the metab-

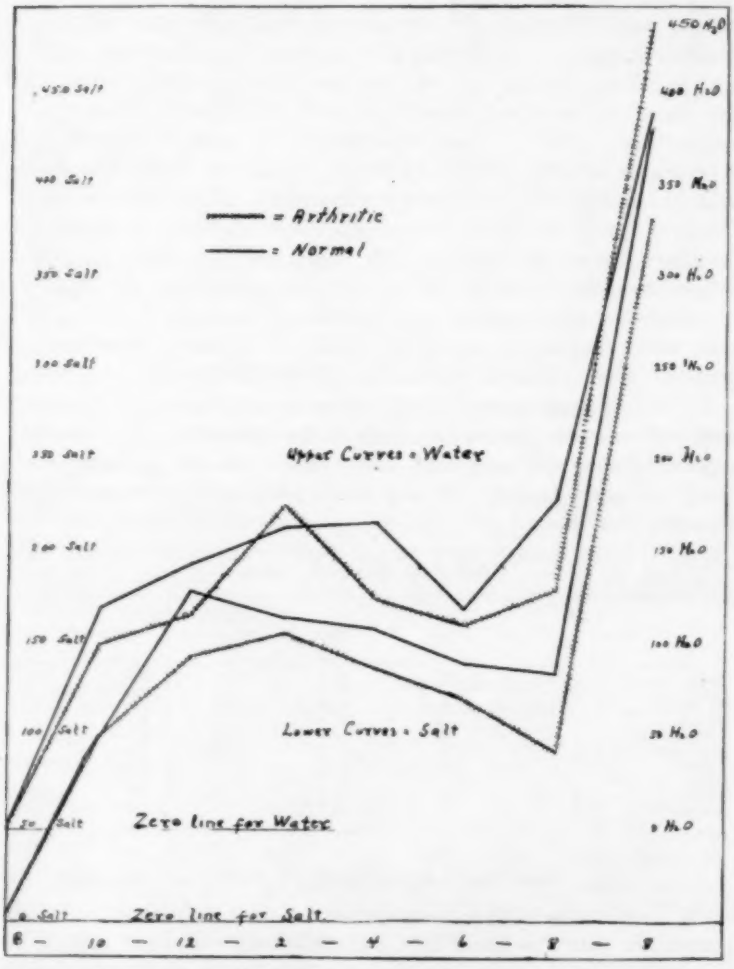

Chart 1.—The salt and water output for normal persons and arthritis patients.

olism of arthritis, such considerations were given added relevance by the evidence at hand regarding blood nitrogen, blood sugar and the influence of a reduced diet in this disease (see sections devoted to these topics). Studies were, therefore, conducted on the total fats

and cholesterol of the fasting blood, using the method of Bloor.[7] Determinations were made on fourteen subjects, but gave, as Table 4 shows, results which fall within the rather wide range attributed to normal values. All degrees of severity of the disease were represented.

TABLE 4.—Blood Lipoids

Name	Case	Date	Total Fat		Cholesterol	
			Blood, per Cent.	Plasma, per Cent.	Blood, per Cent.	Plasma, per Cent.
Robbins	1	1/19	0.668	0.738	0.165	0.137
Hayes	6	1/10	0.616	0.680	0.093	0.082
Jaffy	7	1/19	0.381	0.405	0.079	0.072
McGrann	4	1/19	0.400	0.410	0.080	0.075
Boyd	12	1/ 8	0.650	0.690	0.144	0.109
Hinman	11	1/ 6	0.420	0.600	0.078	0.077
Masood	10	1/ 6	0.360	0.483	0.124	0.101
Lowe	14	1/13	0.416	0.440	0.103	0.097
Wason	20	1/29	0.410	0.460	0.097	0.067
Whittington	21	2/ 4	0.378	0.438	0.068	0.075
Oberg	22	2/ 4	0.418	0.444	0.073	0.070
Jansen	48	5/ 5	0.380	0.420	0.086	0.068
Herron	60	5/ 5	0.415	0.448	0.090	0.071
Cotter	55	5/ 5	0.432	0.450	0.095	0.070

THE RENAL FUNCTION

Until the rôle frequently played by focal infections was appreciated, it was long the custom, and still is in many quarters, to attach chief importance to the stimulation of all eliminative functions, particularly those of the skin, as factors in the therapeusis of arthritis. It cannot be denied that there is evidence that such measures play a useful, if limited, rôle, especially in combination with other measures, in cases tending to improve and those in which the basis is laid for convalescence. Their importance per se, however, has possibly been somewhat overestimated. They rarely remove the cause of the disease, and the results attributed to them are sometimes referable to other incidental or intended factors. It is further possible, or even probable, that the measures necessary to promote elimination through the skin depend for their beneficial effect on factors of which the sweating per se is largely an incidental consequence. Efforts at increasing elimination by copious drinking of water, and even by active purgation, have also had large emphasis at many hands, and one patient in the present series had lost 20 pounds in weight from active daily catharsis long continued. The value of compensatory elimination through the skin and bowels in certain nephritic states cannot be doubted, and long ago suggested itself as possibly of value in arthritis. Whether its benefits in arthritis depend on the inability of the kidney to perform its normal functions properly, however, has been the subject of only a limited amount of study.

7. Bloor: J. Biol. Chem. **17**:377, 1914; **23**:317, 1915.

Evidence adduced by one of us[8] (see also chapter on blood nitrogen) as to the renal function in arthritis, when measured by the phenolsulphonephthalein test and the urea and noncoagulable nitrogen of the blood, has indicated no departure from normal as far as these tests are concerned. It seemed advisable, however, to examine the question of renal function from another angle in view of the exceptional number of subjects and their relative freedom from the factors of later life which might cloud the issue.

No attempt will be made here to weigh the values of the various tests of kidney function or their worth in indicating the nature of the underlying pathology. Suffice it, that of the several methods, the

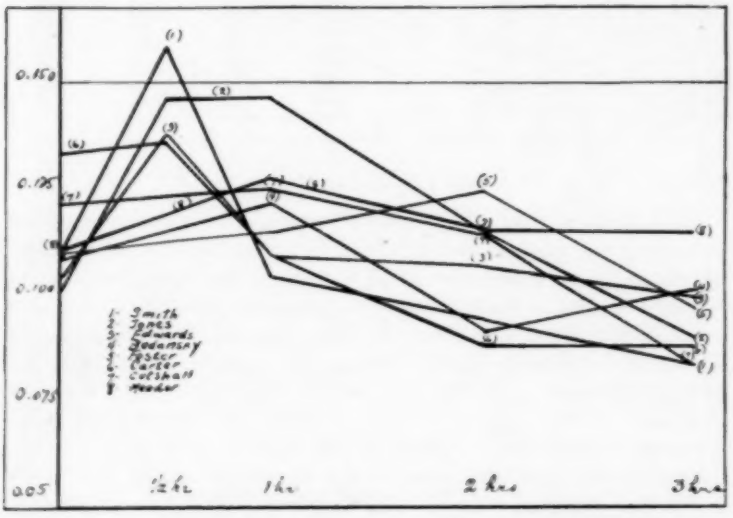

Chart 2.—The curves of sugar tolerance in eight normal individuals. The ordinates are percentage concentrations of blood sugar, the abscissae are time periods of one half, one, two and three hours, respectively. The black transverse line in this and the following charts corresponds to a percentage sugar concentration of 0.150 and is at the approximate upper limit of normality after feeding 100 gm. of glucose. The glucose was ingested immediately after determination of the first point on each curve. The second point was determined one-half or one hour, generally one-half hour, after the first.

method depending on the renal test meal of Hedinger and Schlayer, modified by Mosenthal[9] probably gives the earliest indications of diminished kidney efficiency, and, in addition, has not been applied hitherto to the study of arthritis in any large way. This test depends

8. Pemberton, R.: Am. J. M. Sc. **147**:423 (March) 1914.
9. Mosenthal and Lewis: J. A. M. A. **67**:933, 1916.

on the eliminative response of the kidney to approximately constant amounts of water, salt and nitrogen ingested in a generous mixed dietary of about 2,100 calories. We, therefore, adopted this test as a further means of studying the renal function in a considerable series of arthritics and normal individuals, and followed, with a few modifications, the directions laid down by the authors.

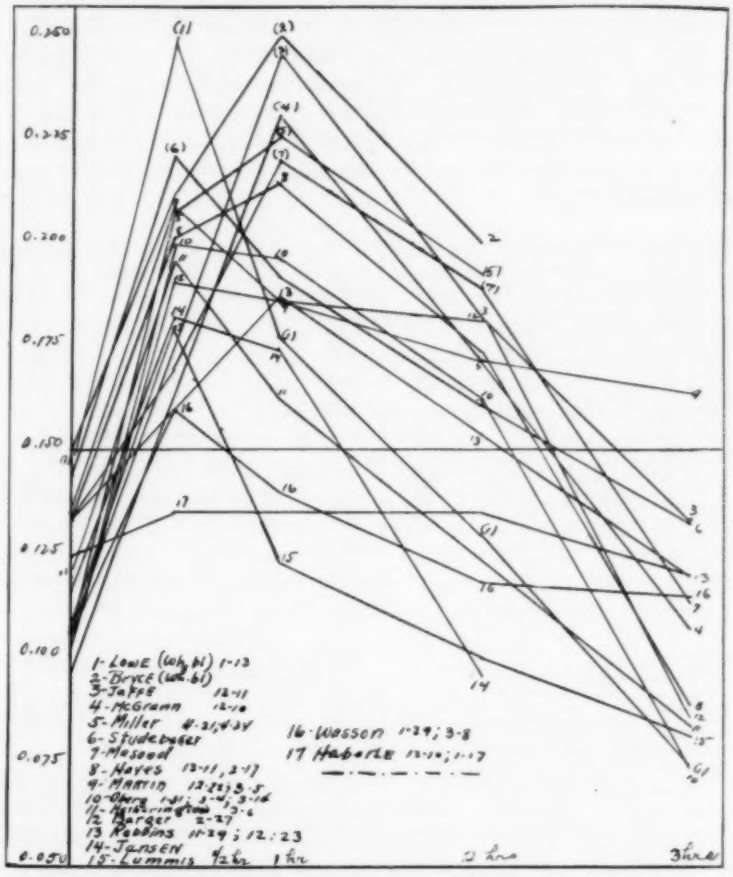

Chart 3.—The lowered sugar tolerance in severe arthritis.

At 8 a. m. the patient emptied the bladder and was then given breakfast; the urine was then collected in two-hour periods up to 8 p. m. The midday and evening meals were taken at 12 noon and 6 p. m., respectively. The night urine from 8 p. m. to 8 a. m. was collected in one specimen. The urine was examined in the usual way

for volume, specific gravity and chlorids, and the total nitrogen was determined on the composite twenty-four-hour amount.

During the day of the test the patient was required to keep as quiet as possible, and all medication and physiotherapy which might vitiate the results were omitted. The patient was watched carefully, and results were discarded when there was suspicion that the patient did not follow directions closely. The diet administered was prepared by trained dietitians in the diet kitchen.[9a] Its composition is indicated in Table 5. It corresponds to the so-called "high" protein diet used by Mosenthal, although he has indicated that certain characteristics, as shown "by the specific gravity of all the specimens and the volume of the night urine, are present regardless of the diet and may be regarded as the normal standards by which to judge similar tests in abnormal individuals." [10]

TABLE 5.—Test Diet

Foodstuff	Quantity	Protein, Gm.	Carbohydrate, Gm.	Fat, Gm.	Salt, Gm.	Fluid, C.c.	Calories
Boiled oatmeal	100 gm.	2.80	11.50	0.50	...	.....	62
Sugar	10 gm.	.....	10.00	.....	...	.....	41
Milk	270 c.c.	9.28	13.50	11.00	...	270	196
Bread	60 gm.	5.52	31.86	0.80	...	.....	160
Butter	20 gm.	0.20	16.75	.....	...	.....	158
Salt	2.3 gm.	.....	.....	.....	2.3		
Coffee	160 c.c.	.....	.....	.....	...	160	
Water	200 c.c.	.....	.....	.....	...	200	
Meat soup	180 c.c.	.....	.....	.....	...	180	
Beefsteak	100 gm.	27.60	.....	7.70	...	.....	185
Potato	130 gm.	2.77	32.07	0.20	...	.....	149
Vegetable	100 gm.	0.70	2.00	1.00	...	.....	21
Bread	60 gm.	5.52	31.86	0.80	...	.....	160
Butter	20 gm.	0.20	.....	16.75	...	.....	158
Sugar	10 gm.	.....	10.00	.....	...	.....	41
Milk	20 c.c.	0.64	1.00	0.80	...	.....	14
Pudding	100 gm.	6.46	25.80	5.04	...	.....	179
Water	250 c.c.	.....	.....	.....	...	250	
Tea	180 c.c.	.....	.....	.....	...	180	
Salt	2.3 gm.	.....	.....	.....	2.3		
Eggs	2 each	13.20	.....	12.00	...	.....	166
Bread	60 gm.	5.52	31.86	0.80	...	.....	160
Butter	20 gm.	0.20	.....	16.75	...	.....	158
Tea	180 c.c.	.....	.....	.....	...	180	
Sugar	10 gm.	.....	10.00	.....	...	.....	41
Milk	20 c.c.	0.64	1.00	0.80	...	.....	14
Fruit							
Water	300 c.c.	.....	.....	.....	...	300	
Salt	2.3 gm.	.....	.....	.....	2.3		
Total	.....	82.2 (13 gm. N)	212.5	91.7	...	1,720	2,064

It became early apparent, in studying small departures from the normal, that it was desirable to establish our own standards of normality under the local conditions presenting, and we, therefore, conducted observations under identical circumstances on a series of

9a. Appreciation should be expressed for the skilful cooperation of Miss Martha Ziegler.

10. Mosenthal: Arch. Int. Med. **12**:770 (Dec.) 1918.

nine presumably normal men mostly from the medical corps attached to the hospital. These individuals were intelligent and trained subjects accustomed to careful cooperation.

TABLE 6.—MEAN WATER AND SALT EXCRETION BY PERIODS *

Period	Water, C.c.		Salt, Gm.	
	Normal	Arthritic	Normal	Arthritic
8-10	118	101	1.00	1.02
10-12	143	117	1.79	1.45
12- 2	161	174	1.64	1.56
2- 4	165	124	1.59	1.37
4- 6	119	111	1.41	1.20
6- 8	179	132	1.36	0.92
8-10	391	441	4.22	3.83
Total	1,279	1,201	13.12	11.36

* The normal figures are based on the mean figures for nine cases. The arthritic figures are based on the mean figures for thirty cases.

Examination of the results of this test reveals that individual cases of arthritis occasionally show low outputs of water for the twenty-four-hour period, and sometimes retention of salt and nitrogen. The mean water output of twenty-nine arthritics shows a normal total volume of 1,200 c.c.; the mean salt output shows an approximately normal amount of 11.36 gm., and the mean nitrogen output shows an approximately normal amount of 11.1 gm. The rather wide range allowed to normality makes it difficult to attach importance to small departures from it. Comparison of these figures with analogous figures obtained from the normal cases studied under similar conditions, however, shows on the part of the arthritics a mean water output of about the same volume as the normals, a mean nitrogen output slightly smaller in amount, 11.1 gm., as against 12.2 gm., and a rather lower mean salt output of 11.36 gm., as against 13.12 gm. for the normals. The chart represents this graphically.[10a]

The percentage salt concentration for arthritics as compared with normals is less in four of the seven periods of the test. It is greater in two and practically the same in one. The amount by which it is less than in the normal cases is most marked in the night urine. The specific gravity is generally high. The maximum specific gravity is always above the minimum figures of from 1.018 to 1.020 accorded to normals under the conditions of the tests. The work of Mosenthal indicates that the variation in specific gravity for normals should be greater than 9 degrees. The variation of the specific gravity is less than 9 degrees in nine of the twenty-nine tests, but Mosenthal emphasizes that this is of little or no significance if the specific gravity is above 1.010, as was the case in every instance. In three of these cases the variation was more than 9 degrees when the test was repeated.

10a. This and the following charts were prepared by Sergt. Meyer Bodansky, M. C., U. S. Army.

The variation was less than 9 degrees in Case 22, Case 53, Case 52, IV/2 (not corroborated in test of IV/3), Case 71, IV/2 (not corroborated in test of V/2), Case 57, IV/17 (not corroborated in test of IV/29), Case 48, Case 46, Case 55 and Case 62. One normal control gave a variation of less than 9 degrees, with a high specific gravity. The volume of the night urine was less than 750 c.c. in all cases but one (Case 56), but in this instance the specific gravity and other elements were all normal. Severe cases of advanced type may repeatedly

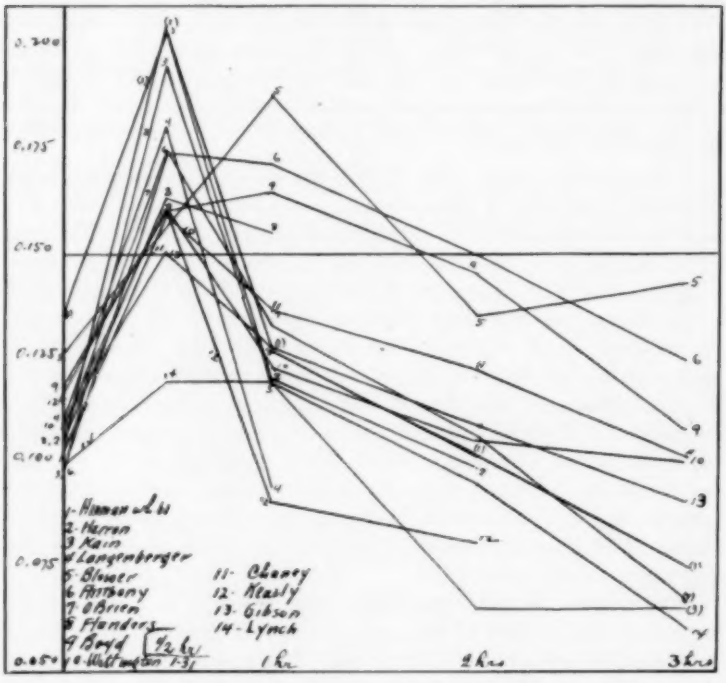

Chart 4.—Lowered sugar tolerance in arthritis of moderate severity. This chart and Chart 5 tend to show that the lowered sugar tolerance is somewhat proportional to the severity of the arthritis. Most of the curves are importantly lower than in Chart 2.

give figures by whatever standards entirely within normal limits as respects all elements of the test. (Compare Case 14, March 11 and April 28; Case 7, Case 6, Case 52, Case 46 and Case 60.)

Observations were also conducted on the phenolsulphonephthalein elimination, but the results were all normal and coincided with the normal figures for this test previously recorded.[11] Hanzlik,[12] in study-

11. Pemberton, R.: Am. J. M. Sc. **147**: 423 (March) 1914.
12. Hanzlik: J. Pharmacol. & Exper. Therap. **9**:263 (Feb.) 1917.

ing the salicylates, has found phenolsulphonephthalein values ranging from 55 to 75 per cent., and has concluded that renal functional efficiency is quite as good in the rheumatic as in the normal individual.

The above findings should be weighed in connection with the estimations of blood urea and noncoagulable nitrogen which were in a large series, with two exceptions, entirely within normal limits, as noted under the section dealing with this topic.

Of the more than 400 cases of arthritis studied by us in which all types and degrees were represented, only six patients had a true nephritis. The factors making for nephritis under conditions of warfare need no emphasis here, and sufficed to account for these cases.

It is to be noted, that whereas the average fasting level for blood sugar for the whole group of arthritics is slightly higher than that for normals (0.115 per cent. as against 0.109 per cent. or lower), the fasting level of blood urea and nitrogen for arthritics is the same as for normals. It would perhaps be of some value to conduct urea feeding tests comparable to the glucose tolerance tests with examination of the level of blood nitrogen and urea at frequent intervals after ingestion. It is to be doubted whether the disturbance which affects the utilization or removal of the glucose of the blood stream described in the next section, is confined in its influence to carbohydrate alone. There are reasons for believing it to be the expression of a widespread function in which the fats and, possibly in some degree, the nitrogenous elements may be involved.

TABLE 7.—Total Urinary Nitrogen

Arthritics				Normals	
Lt. Lynch	13.6	Langenberger	10.2	Pittsley	14.2
Hetherington	14.7	Tingue	10.7	Parsons	14.8
Cotter	12.4	McIntyre	10.3	Edwards	11.7
Barger	12.8	Chaney	11.9	Bollman	12.9
Langenberger	10.5	Crawford	7.1	Bodansky	11.5
Kearly	12.3	Keyes	7.2	Stricker	12.3
Hickey	9.4	Jordan	11.9	Swenarton	10.6
Jansen	11.4	Herron	12.4		
Lowe	14.0	McKenzie	7.9		
Mean (of 18) 11.1				Mean (of 7) 12.2	

To summarize: Charts constructed to show the response of arthritics, as compared with normals under similar conditions, to the so-called nephritis test meal indicate a very slight lag in the elimination of water, nitrogen and particularly of salt. This is hardly to be appreciated when viewed only in the light of the rather widely varying figures ascribed to normals at large. It seems fair to conclude in conjunction with the normal values found for urea and nonprotein nitrogen of the fasting blood that there is no marked dislocation of renal function in chronic arthritis, though this function may be slightly lowered in some cases.

TABLE 8.—Data as to Volume, Specific Gravity, Sodium Chlorid and Nitrogen in Indiviual Cases

Name	Date	Time	Volume, C.c.	Specific Gravity	NaCl per Cent.	NaCl Gm.	Total N, Gm.
Oberg	2/26	8-10 a. m.	82	1.002	0.90	0.74	
		10-12 a. m.	140	1.003	0.89	1.24	
		12- 2 p. m.	56	1.005	1.06	0.59	
		2- 4 p. m.	118	1.004	1.20	1.42	
		4- 6 p. m.	157	1.028	0.86	1.34	
		6- 8 p. m.	55	1.030	0.98	0.54	
		Night*	354	1.032	1.06	3.75	
Total	....	.....	962	.....	....	9.62	
Jaffy	3/20	8-10 a. m.	121	1.026	0.86	1.04	
		10-12 a. m.	92	1.035	1.30	1.20	
		12- 2 p. m.	356	1.020	0.41	1.44	
		2- 4 p. m.	156	1.060	0.86	1.33	
		4- 6 p. m.	94	1.035	0.96	0.90	
		6- 8 p. m.	262	1.021	0.49	1.28	
		Night	490	1.026	0.67	3.29	
Total	....	.....	1,571	.....	....	10.48	
Lowe (Omitted from average)	2/5	8-10 a. m.	60	1.031	1.40	0.84	
		10-12 a. m.	92	1.035	1.71	1.57	
		12- 2 p. m.	63	1.042	1.47	0.93	
		2- 4 p. m.	108	1.036	1.23	1.23	
		4- 6 p. m.	89	1.038	1.20	1.08	
		6- 8 p. m.	51	1.037	1.16	0.59	
		Night	297	1.033	0.81	2.41	
Total	....	.....	760	.....	....	8.74	
McGrann	2/5	8-10 a. m.	174	1.016	0.28	0.49	
		10-12 a. m.	180	1.019	0.52	0.94	
		12- 2 p. m.	309	1.019	0.57	1.71	
		2- 4 p. m.	142	1.060	1.06	1.51	
		4- 6 p. m.	144	1.050	1.05	1.51	
		6- 8 p. m.	163	1.021	0.42	0.69	
		Night	321	1.030	0.50	1.64	
Total	....	.....	1,431	.....	....	8.49	
Hayes	2/5	8-10 a. m.	200	1.017	0.48	1.72	
		10-12 a. m.	295	1.018	0.735	2.17	
		12- 2 p. m.	340	1.017	0.40	1.36	
		2- 4 p. m.	95	1.030	0.90	0.86	
		4- 6 p. m.	102	1.029	0.98	1.00	
		6- 8 p. m.	65	1.029	1.30	0.83	
		Night	285	1.035	0.92	2.62	
Total	....	.....	1.542	.....	....	10.56	
Barger	2/5	8-10 a. m.	73	1.027	1.07	0.78	
		10-12 a. m.	80	1.035	1.47	1.18	
		12- 2 p. m.	130	1.028	1.02	1.33	
		2- 4 p. m.	91	1.031	1.00	0.94	
		4- 6 p. m.	62	1.039	1.22	0.76	
		6- 8 p. m	212	1.021	0.54	1.14	
		Night	325	1.032	1.04	3.38	
Total	....	.....	973	.....	....	9.51	
Lowe	3/11	8-10 a. m.	102	1.028	1.38	1.36	
		10-12 a. m.	142	1.027	1.36	1.93	
		12- 2 p. m.	150	1.024	0.93	1.39	
		2- 4 p. m.	150	1.025	0.83	1.24	
		4- 6 p. m.	110	1.027	0.93	1.02	
		6- 8 p. m.	62	1.023	0.77	0.48	
		Night	530	1.021	0.53	2.81	
Total	....	.....	1,246	.....	....	10.23	

* From 8 p. m. to 8 a. m.

TABLE 8.—Data as to Volume, Specific Gravity, Sodium Chlorid and Nitrogen in Individual Cases—(*Continued*)

Name	Date	Time	Volume, C.c.	Specific Gravity	NaCl per Cent.	NaCl Gm.	Total N, Gm.
Lau	3/25	8–10 a. m.	200	1.025	1.14	2.28	
		10–12 a. m.	112	1.030	1.50	1.68	
		12– 2 p. m.	116	1.030	1.27	1.47	
		2– 4 p. m.	156	1.031	1.20	1.86	
		4– 6 p. m.	60	1.025	0.72	0.43	
		6– 8 p. m.	112	1.030	0.93	1.04	
		Night	100	1.034	1.18	1.18	
Total	....	.....	855	.....	....	9.94	
Brake	3/25	8–10 a. m.	150	1.035	1.69	2.54	
		10–12 a. m.	100	1.033	1.88	1.88	
		12– 2 p. m.	115	1.032	1.90	2.19	
		2– 4 p. m.	120	1.037	1.75	2.10	
		4– 6 p. m.	80	1.035	1.69	1.35	
		6– 8 p. m.	175	1.019	0.63	1.10	
		Night	515	1.025	0.87	4.48	
Total	....	.....	1,255	.....	....	15.64	
Mrs. Kain	4/1	8–10 a. m.	75	1.000	1.00	0.75	
		10–12 a. m.	75	1.035	1.48	1.11	
		12– 2 p. m.	100	1.033	1.34	1.34	
		2– 4 p. m.	100	1.033	1.24	1.24	
		4– 6 p. m.	48	1.029	1.22	0.59	
		6– 8 p. m.	113	1.022	1.28	1.45	
		Night	430	1.028	1.14	4.90	
Total	....	.....	941	.....	....	11.38	
Lt. Lynch	4/2	8–10 a. m.	54	1.029	1.14	0.62	
		10–12 a. m.	100	1.029	1.13	1.13	
		12– 2 p. m.	120	1.030	1.26	1.51	
		2– 4 p. m.	92	1.033	1.35	1.24	
		4– 6 p. m.	141	1.031	1.34	1.89	
		6– 8 p. m.	95	1.030	0.82	0.78	
		Night	670	1.035	0.92	6.15	
Total	....	.....	1,272	.....	....	13.02	
Lt. Lynch	4/3	8–10 a. m.	93	1.025	1.38	1.29	
		10–12 a. m.	135	1.026	1.50	2.02	
		12– 2 p. m.	130	1.027	1.40	1.82	
		2– 4 p. m.	110	1.030	1.42	1.84	
		4– 6 p. m.	135	1.028	1.18	1.59	
		6– 8 p. m.	235	1.020	0.54	1.27	
		Night	695	1.023	1.04	7.23	
Total	....	.....	1,533	.....	....	17.06	13.6
Crawford	4/2	8–10 a. m.	35	1.031	0.74	0.26	
		10–12 a. m.	38	1.034	0.90	0.34	
		12– 2 p. m.	67	1.033	0.84	0.56	
		2– 4 p. m.	180	1.035	0.86	1.69	
		4– 6 p. m.	101	1.030	1.30	1.37	
		6– 8 p.m.	122	1.030	1.46	1.78	
		Night	545	1.030	1.64	8.95	
Total	....	.....	1.094	.....	....	14.86	
Jansen	4/2	8–10 a. m.	50	1.035	1.34	0.67	
		10–12 a. m.	125	1.035	1.60	2.00	
		12– 2 p. m.	148	1.035	1.52	2.24	
		2– 4 p. m.	70	1.040	1.56	1.09	
		4– 6 p. m.	70	1.040	1.70	1.19	
		6– 8 p. m.	60	1.030	1.64	0.98	
		Night	302	1.039	1.36	4.10	
Total	....	.....	825	.....	....	12.27	

TABLE 8.—Data as to Volume, Specific Gravity, Sodium Chlorid and Nitrogen in Individual Cases—(*Continued*)

Name	Date	Time	Volume, C.c.	Specific Gravity	NaCl per Cent.	NaCl Gm.	Total N, Gm.
Hetherington	4/3	8-10 a. m.	50	1.028	1.50	0.75	
		10-12 a. m.	175	1.029	1.46	2.56	
		12- 2 p. m.	200	1.030	1.60	3.84	
		2- 4 p. m.	125	1.022	1.50	1.88	
		4 -6 p. m.	160	1.023	1.54	2.46	
		6- 8 p. m.	135	1.032	1.48	2.00	
		Night	455	1.033	1.40	6.35	
Total	....	.....	1,362	.....	....	19.84	14.7
Cotter	4/7	8-10 a. m.	106	1.031	1.76	1.87	
		10-12 a. m.	126	1.032	1.92	2.42	
		12- 2 p. m.	164	1.031	1.85	3.20	
		2- 4 p. m.	94	1.037	1.85	1.74	
		4- 6 p. m.	100	1.038	1.92	1.92	
		6- 8 p. m.	150	1.036	1.70	2.55	
		Night	350	1.039	1.54	5.40	
Total	....	.....	1.090	.....	....	19.10	12.4
Barger	4/15	8-10 a. m.	96	1.026	1.55	1.49	
		10-12 a. m.	98	1.026	1.67	1.64	
		12- 2 p. m.	150	1.028	1.28	1.92	
		2- 4 p. m.	104	1.032	1.31	1.37	
		4- 6 p. m.	62	1.067	1.43	0.89	
		6- 8 p. m.	97	1.026	0.89	0.87	
		Night	315	1.030	0.94	2.96	
Total	....	.....	922	.....	....	11.13	12.8
Langenberger	4/17	8-10 a. m.	73	1.026	0.86	0.63	
		10-12 a. m.	75	1.027	0.90	0.68	
		12- 2 p. m.	116	1.026	1.12	1.30	
		2- 4 p. m.	200	1.025	1.08	2.16	
		4- 6 p. m.	155	1.024	0.86	1.33	
		6- 8 p. m.	242	1.019	0.44	1.07	
		Night	430	1.024	0.66	2.84	
Total	....	.....	1,291	.....	....	10.01	10.5
Kearly	4/19	8-10 a. m.	54	1.030	1.24	0.67	
		10-12 a. m.	98	1.029	1.40	1.37	
		12- 2 p. m.	242	1.019	0.56	1.36	
		2- 4 p. m.	308	1.024	0.82	1.71	
		4- 6 p. m.	106	1.029	1.05	1.12	
		6- 8 p. m.	180	1.012	0.12	0.22	
		Night	1,056	1.012	0.46	4.86	
Total	....	.....	1,944	.....	....	11.28	12.2
Miss Hickey	4/16	8-10 a. m.	98	1.020	1.00	0.98	
		10-12 a. m.	120	1.020	1.10	1.32	
		12- 2 p. m.	216	1.014	0.54	1.16	
		2- 4 p. m.	172	1.023	1.12	1.93	
		4- 6 p. m.	122	1.021	0.86	1.14	
		6- 8 p. m.	74	1.019	0.49	0.36	
		Night	400	1.023	0.64	3.14	
Total	....	.....	1,300	.....	....	9.93	9.4
Jansen	4/28	8-10 a. m.	80	1.031	1.42	1.17	
		10-12 a. m.	115	1.029	1.52	1.75	
		12- 2 p. m.	145	1.030	1.66	2.40	
		2- 4 p. m.	122	1.026	1.30	1.59	
		4- 6 p. m.	152	1.024	1.00	1.52	
		6- 8 p. m.	180	1.020	0.58	1.04	
		Night	265	1.032	0.80	2.12	
Total	....	.....	1,059	.....	....	11.59	11.4

TABLE 8.—Data as to Volume, Specific Gravity, Sodium Chlorid and Nitrogen in Individual Cases—(*Continued*)

Name	Date	Time	Volume, C.c.	Specific Gravity	NaCl per Cent.	NaCl Gm.	Total N, Gm.
Lowe	4/28	8-10 a. m.	87	1.035	1.68	1.46	
		10-12 a. m.	135	1.030	1.66	2.24	
		12- 2 p. m.	125	1.034	1.64	2.05	
		2- 4 p. m.	125	1.029	1.32	1.65	
		4- 6 p. m.	90	1.034	1.10	0.99	
		6- 8 p. m.	95	1.026	0.60	0.57	
		Night	625	1.021	0.58	3.62	
Total	....	.....	1,283	.....	....	12.58	14.0
Langenberger	4/29	8-10 a. m.	115	1.027	1.10	1.27	
		10-12 a. m.	115	1.020	0.90	1.04	
		12- 2 p. m.	180	1.018	0.80	1.44	
		2- 4 p. m.	185	1.014	0.40	0.74	
		4- 6 p. m.	175	1.016	0.66	1.15	
		6- 8 p. m.	180	1.020	0.88	1.58	
		Night	215	1.030	1.20	2.58	
Total	....	.....	1,165	.....	....	9.80	10.2
Tingue	5/1	8-10 a. m.	70	1.035	1.50	1.05	
		10-12 a. m.	75	1.035	1.84	1.38	
		12- 2 p. m.	65	1.032	1.12	0.73	
		2- 4 p. m.	100	1.031	1.14	1.14	
		4- 6 p. m.	98	1.029	0.94	0.92	
		6- 8 p. m.	75	1.032	0.68	0.51	
		Night	550	1.021	0.70	3.85	
Total	....	.....	1.033	.....	....	9.58	10.7
McIntyre	5/2	8-10 a. m.	85	1.038	1.62	1.38	
		10-12 a. m.	70	1.069	1.66	1.16	
		12- 2 p. m.	120	1.035	1.22	1.47	
		2- 4 p. m.	60	1.036	1.26	0.76	
		4- 6 p. m.	115	1.036	1.02	1.17	
		6- 8 p. m.	145	1.019	0.32	0.47	
		Night	260	1.040	0.98	2.55	
Total	....	.....	855	.....	....	8.96	10.3
Chaney	5/2	8-10 a. m.	85	1.030	0.78	0.66	
		10-12 a. m.	75	1.034	1.18	0.89	
		12- 2 p. m.	170	1.017	0.74	1.26	
		2- 4 p. m.	175	1.023	0.78	1.37	
		4- 6 p. m.	185	1.025	1.02	1.88	
		6- 8 p. m.	175	1.014	0.24	0.42	
		Night	380	1.032	0.78	2.96	
Total	....	.....	1,245	.....	....	9.44	11.9
Crawford	5/2	8-10 a. m.	175	1.014	0.26	0.46	
		10-12 a. m.	170	1.019	0.56	0.95	
		12- 2 p. m.	155	1.016	0.42	0.65	
		2- 4 p. m.	50	1.030	0.78	0.39	
		4- 6 p. m.	145	1.024	0.72	1.05	
		6- 8 p. m.	180	1.016	0.30	0.54	
		Night	640	1.018	0.54	3.46	
Total	....	.....	1,515	.....	....	7.50	7.1
Lt. Keyes	5/2	8-10 a. m.	45	1.030	0.80	0.36	
		10-12 a. m.	100	1.028	1.22	1.22	
		12- 2 p. m.	95	1.028	1.20	1.14	
		2- 4 p. m.	120	1.029	0.86	1.03	
		4- 6 p. m.	130	1.027	1.06	1.38	
		6- 8 p. m.	60	1.039	0.80	0.48	
		Night	230	1.034	1.00	2.30	
Total	....	.....	780	.....	....	7.91	7.2

TABLE 8.—Data as to Volume, Specific Gravity, Sodium Chlorid and Nitrogen in Individual Cases—(*Continued*)

Name	Date	Time	Volume, C.c.	Specific Gravity	NaCl per Cent.	NaCl Gm.	Total N, Gm.
Lt. Jordan	5/2	8-10 a. m.	105	1.020	0.28	0.29	
		10-12 a. m.	135	1.025	1.02	1.38	
		12- 2 p. m.	480	1.013	0.28	1.34	
		2- 4 p. m.	115	1.030	0.98	1.13	
		4- 6 p. m.	100	1.032	1.06	1.06	
		6- 8 p. m.	135	1.021	0.48	0.65	
		Night	260	1.035	0.70	1.82	
Total	....	.....	1,330	.....	....	7.67	11.6
Herron	5/2	8-10 a. m.	95	1 033	1.56	1.48	
		10-12 a. m.	100	1.032	1.68	1.68	
		12- 2 p. m.	335	1.019	0.70	2.34	
		2- 4 p. m.	110	1.027	1.12	1.23	
		4- 6 p. m.	65	1.034	1.06	0.69	
		6- 8 p. m.	80	1.035	0.94	0.75	
		Night	725	1.019	0.76	5.50	
Total	....	.....	1,510	.....	....	13.67	12.4
McKenzie	5/4	8-10 a. m.	32	1.025	0.74	0.24	
		10-12 a. m.	120	1.036	0.92	1.10	
		12- 2 p. m.	65	1.026	0.52	0.34	
		2- 4 p. m.	115	1.030	0.94	1.08	
		4- 6 p. m.	60	1.030	0.64	0.39	
		6- 8 p. m.	58	1.030	0.46	0.27	
		Night	410	1.025	1.02	4.18	
Total	....	.....	860	.....	....	7.60	8.1

NORMALS

Lynch	3/28	8-10 a. m.	122	1.028	1.60	1.94	
		10-12 a. m.	174	1.025	1.65	2.87	
		12- 2 p. m.	186	1.021	0.92	1.71	
		2- 4 p. m.	300	1.017	0.62	2.23	
		4- 6 p. m.	182	1.024	1.04	1.89	
		6- 8 p. m.	202	1.021	0.86	1.74	
		Night	315	1.031	0.76	2.85	
Total	....	.....	1,601	.....	....	15.23	
Jones	3/24	8-10 a. m.	48	1.037	1.22	0.60	
		10-12 a. m.	87	1.035	1.66	1.47	
		12- 2 p. m.	170	1.031	1.30	2.01	
		2- 4 p. m.	180	1.030	0.96	1.70	
		4- 6 p. m.	116	1.036	1.26	1.65	
		6- 8 p. m.	276	1.018	0.46	1.27	
		Night	440	1.032	1.20	3.19	
Total	....	.....	1,317	.....	....	13.14	
Bollman	....	8-10 a. m.	62	1.035	0.90	0.56	
		10-12 a. m.	102	1.037	1.47	1.50	
		12- 2 p. m.	174	1.030	1.62	2.83	
		2- 4 p. m.	116	1.036	1.55	1.80	
		4- 6 p. m.	72	1.041	1.43	1.03	
		6- 8 p. m.	91	1.040	1.47	1.34	
		Night	295	1.040	1.16	3.13	
Total	....	.....	912	.....	....	12.19	12.9

TABLE 8.—Data as to Volume, Specific Gravity, Sodium Chlorid and Nitrogen in Individual Cases—(*Continued*)
Normals—*Continued*

Name	Date	Time	Volume, C.c.	Specific Gravity	NaCl per Cent.	NaCl Gm.	Total N, Gm.
Bodansky	....	8-10 a. m.	106	1.081	1.76	1.87	
		10-12 a. m.	126	1.082	1.92	2.42	
		12- 2 p. m.	164	1.081	1.85	3.20	
		2- 4 p. m.	94	1.037	1.85	1.74	
		4- 6 p. m.	100	1.038	1.92	1.92	
		6- 8 p. m.	150	1.036	1.70	2.55	
		Night	350	1.039	1.54	5.40	
Total	....	.....	1,000	.....	....	19.10	12.35
Stricker	4/16	8-10 a. m.	185	1.017	0.40	0.74	
		10-12 a. m.	225	1.021	0.62	1.40	
		12- 2 p. m.	330	1.015	0.28	0.92	
		2- 4 p. m.	275	1.020	0.70	1.93	
		4- 6 p. m.	165	1.024	0.94	1.55	
		6- 8 p. m.	310	1.017	0.40	1.24	
		Night	380	1.032	1.18	4.48	
Total	....	.....	1,870	.....	....	12.26	12.4
Parsons	....	8-10 a. m.	95	1.022	0.34	0.32	
		10-12 a. m.	130	1.029	1.04	1.25	
		12- 2 p. m.	83	1.031	0.96	0.82	
		2- 4 p. m.	130	1.030	1.32	1.74	
		4- 6 p. m.	130	1.028	0.88	1.14	
		6- 8 p. m.	150	1.022	0.50	0.75	
		Night	325	1.032	1.12	3.64	
Total	....	.....	1,063	.....	....	9.66	11.8
Pittsley	....	8-10 a. m.	200	1.030	0.62	1.80	
		10-12 a. m.	175	1.025	1.12	1.98	
		12- 2 p. m.	75	1.033	0.98	0.74	
		2- 4 p. m.	105	1.034	1.14	1.20	
		4- 6 p. m.	140	1.031	1.30	1.82	
		6- 8 p. m.	170	1.025	0.90	1.53	
		Night	385	1.030	0.92	3.54	
Total	....	.....	1,340	.....	....	12.59	14.2
Edwards	4/18	8-10 a. m.	48	1.032	1.54	0.74	
		10-12 a. m.	108	1.033	1.70	1.84	
		12- 2 p. m.	168	1.031	1.60	2.72	
		2- 4 p. m.	104	1.032	1.42	1.48	
		4- 6 p. m.	92	1.040	1.56	1.44	
		6- 8 p. m.	128	1.036	1.37	1.75	
		Night	575	1.026	1.14	6.56	
Total	....	.....	1,220	.....	....	16.47	11.7
Swenarton	5/10	8-10 a. m.	150	1.027	0.98	1.47	
		10-12 a. m.	195	1.030	1.00	1.95	
		12- 2 p. m.	250	1.021	0.54	1.35	
		2- 4 p. m.	130	1.030	0.70	0.91	
		4- 6 p. m.	100	1.032	1.06	1.06	
		6- 8 p. m.	240	1.029	0.26	0.62	
		Night	510	1.026	0.64	3.26	
Total	....	.....	1,575	.....	....	10.62	13.5

TABLE 9.—Percentage Salt Concentration of Arthritics as Compared with Normals

Period	Normal	Arthritic
8-10 a. m.	0.85	1.01
10-12 a. m.	1.25	1.24
12- 2 p. m.	1.02	0.89
2- 4 p. m.	0.98	1.10
4- 6 p. m.	1.18	1.06
6- 8 p. m.	0.76	0.70
Night	1.11	0.87

THE BLOOD SUGAR[13]

It has been shown by one of us[14] that there is in a considerable percentage of cases of chronic arthritis a definite relation between the intake of food on the one hand, and the incidence or perpetuation of symptoms of the disease on the other. This relation is best illustrated by the fact that the institution of a reduced diet in appropriate cases may be followed by marked benefit. Of the three foodstuffs, the evi-

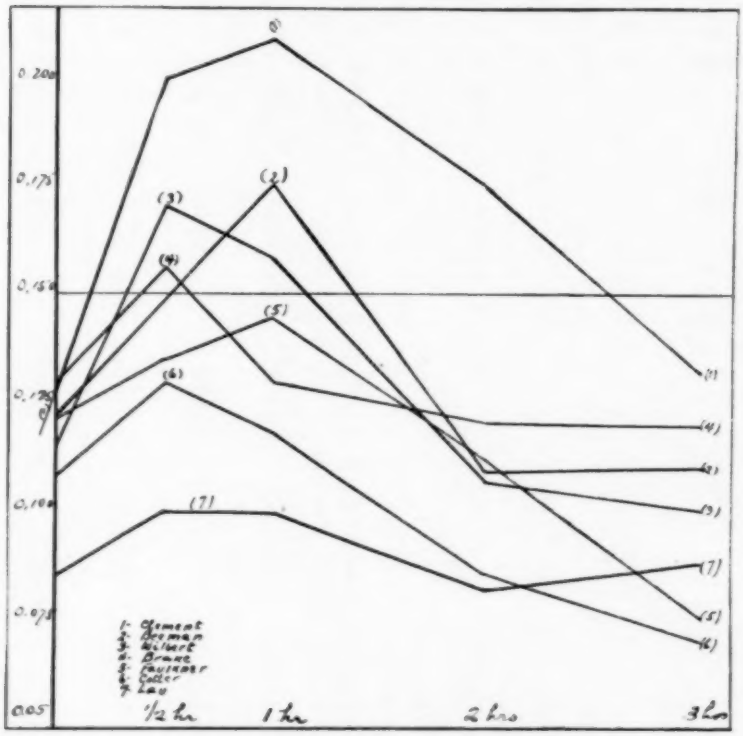

Chart 5.—The sugar tolerance in mild arthritis.

dence at hand, although not yet complete, has indicated that carbohydrate is most concerned in this connection. It became pertinent,

13. In addition to a report as a whole of the present studies on arthritis in the army, made before the Section on Medicine of the American Medical Association, Atlantic City, N. J., June 12, 1919, the findings regarding the blood sugar were reported in fuller detail than was possible before the American Society for Clinical Investigation, Atlantic City, N. J., June 14, 1919.

14. Pemberton, R.: The Metabolism and Treatment of Rheumatoid Arthritis, Am. J. M. Sc. **153**:678 (May) 1917.

therefore, to determine, if possible, in the present large series, whether there is a difficulty in the metabolism of carbohydrate, and to this end studies were carried out in sixty cases of arthritis on the fasting level of the blood sugar and on the response of these cases to the so-called glucose tolerance test.

Jacobsen[15] published studies on the effects of foodstuffs on the blood sugar, using the microchemical method of Bang. Adopting the principle of this method, but directing it toward the study of the carbohydrate tolerance in a variety of conditions, and using the Lewis-Benedict method for blood sugar as being better adapted to clinical use, Hamman and Hirschman[16] opened up an important field of investigation. Janney and Isaacson[17] and others have also contributed to this subject, until there has grown up a considerable and increasing literature devoted to it. The earlier method of determining sugar tolerance by estimations of the urinary sugar only has now been substituted by a combination of the two methods. One hundred and nine glucose tolerance tests were conducted by us in the present series, apart from a considerable number of isolated observations on the fasting blood sugar.

TECHNIC

The Benedict[18] modification of the Lewis-Benedict[19] method for blood sugar was used exclusively. It has, on the whole, proved very satisfactory and well adapted to use in a long series of cases. It may be applied either to whole blood or plasma, but in the analysis of whole blood, certain precautions must be observed to insure removal of interfering substances or results will be obtained which are too high. In the picric acid-sodium picrate solution used for precipitation of the blood protein, the free picric acid alone removes the protein and other interfering substances. The amount of free picric acid is sufficient to clarify the plasma perfectly, but often it is not enough for whole blood which contains more protein. The concentration of free acid in the picric-picrate solution, therefore, must be increased in working with whole blood. This point was noted by Benedict in a recent paper.[20] In the present studies this trouble was encountered and remedied independently of the above publication in substantially the same way that Benedict employed; namely, by the addition of two

15. Jacobsen: Biochem. Ztschr. **56**:47, 1913.
16. Hamman and Hirschman: Arch. Int. Med. **20**:761 (Nov.) 1917.
17. Janney and Isaacson: Arch. Int. Med. **20**:160 (Aug.) 1918.
18. Benedict, S. R.: J. Biol. Chem. **34**:203, 1918.
19. Lewis and Benedict: J. Biol. Chem. **20**:61, 1915.
20. Benedict: J. Biol. Chem. **37**:503, 1919.

drops of 1:2 hydrochloric acid before diluting to 25 c.c. with the picric-picrate solution.[20a]

The glucose tolerance test was conducted according to the method of Hamman and Hirschman:[16]

On the day of the test the patient eats no breakfast.

At 8:30 a. m. samples are obtained of the blood and urine, and the patient is given 100 gm. of glucose in 200 c.c. of water.

At 9:00 a. m. samples are obtained of blood and urine.

At 9:30 a. m. samples are obtained of blood and urine, and the patient is given 200 c.c. of water.

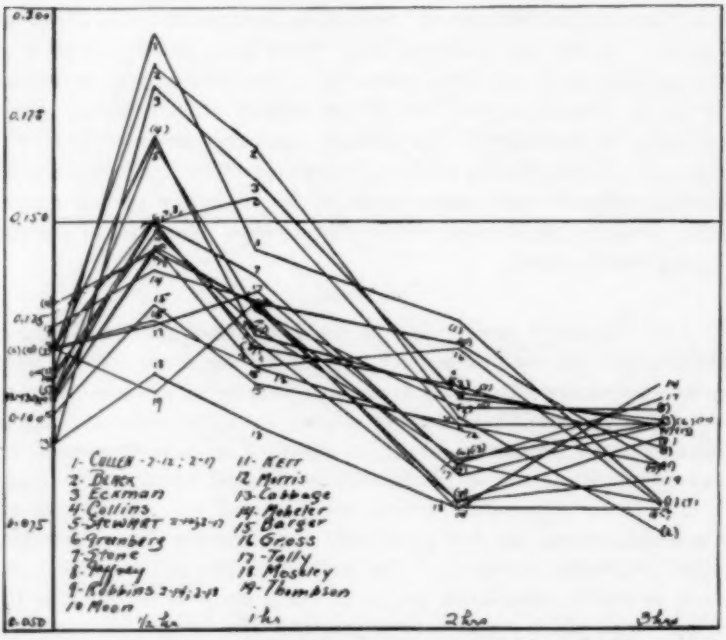

Chart 6.—The sugar tolerance in convalescent arthritics. In 74 per cent. of these cases it was normal.

At 10:30 a. m. samples are taken of blood and urine and the patient is given 200 c.c. of water.

At 11:30 a. m. samples are taken of blood and urine.

The importance of taking the blood on the half hour after the administration of glucose should be emphasized. In the normal man

20a. The question of the rôle played by creatinin in this reaction as pointed out by DeWesselow (Biochem. J. **13**:148, 1919) and others hardly enters here as the contrasts under consideration are frequently very great, they follow immediately on ingestion of glucose and are controlled by fasting levels previously determined.

this period yields the high point in the curve, the reaction is frequently complete at the end of one hour, and in many cases of slightly lowered tolerance the half hour point affords the only characteristic data. Many of the curves show a drop below the normal level at the end of the test, several cases yielding blood and plasma sugar as low as 0.065 per cent. at the end of the third hour.

In the present series the renal threshold for glycosuria fell between 0.17 per cent. and 0.18 per cent., which agrees with the values found by others for the normal kidney, and is something of an argument for

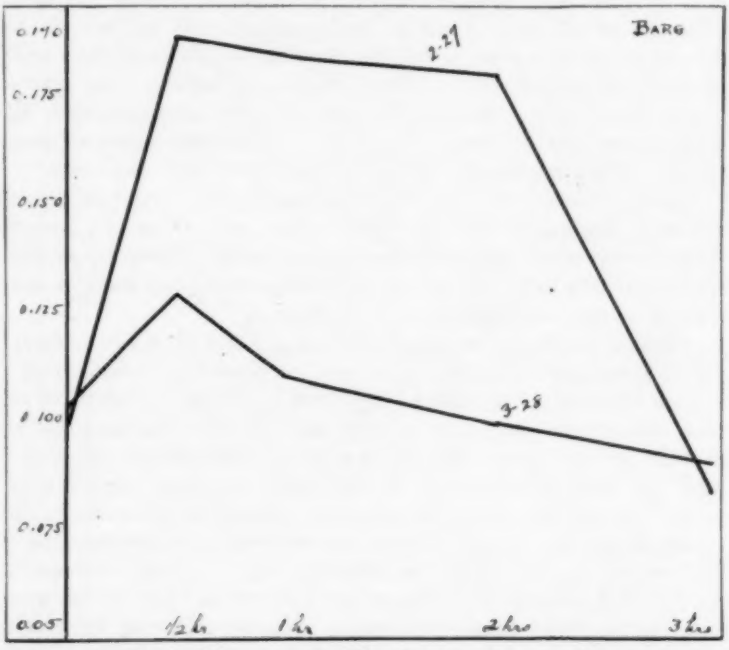

Chart 7.—The striking contrast after fourteen days in the sugar tolerance of a severe arthritic who made an abrupt convalescence following tonsillectomy on March 14, 1919.

the normality of renal function in arthritis, as the threshold may be much higher in true nephritis.

On beginning our work it was soon appreciated that it was necessary to establish our own standards of fasting blood sugar and of glucose tolerance among normal individuals in view of the possibility that local conditions might influence our results, and, therefore, we conducted a series of tests on nine presumably normal persons. The results were found to fall well within the limits indicated by other workers in this field, but as our technic became perfected, we found that the average values were lower than those which we first obtained.

Chart 2 shows the curves obtained in eight normal individuals. The values range from an average fasting level for eleven normals of 0.109 per cent. to an average high point for five normals of 0.140 per cent. at the end of the half hour. The fasting level of sugar for the whole blood in our series falls near the upper limit of the range accorded to normality by Janney and Isaacson [17] (0.085 per cent. to 0.11 per cent.), and is slightly above the level for normals (0.10 per cent.), established by Bang.[21]

It is pertinent to note here that single observations on the fasting level of blood sugar are open to some disturbance, possibly subjective influence, on the part of the person examined, and we were led to discard as erroneous not a few figures in cases which further study proved to be normal. By and large, the glucose tolerance test appears to give results more constantly indicative of conditions disturbing the blood sugar than do single observations. Abnormal responses occasionally follow apparently normal fasting figures and vice versa.

Glucose tolerance tests were then conducted on a series of chronic arthritics, beginning with the worst types, and at once it became apparent that there was in most of them a marked difference in their response to this test. This led us to extend our observations to a large number of cases representative of all types.

Chart 3 shows the response obtained in cases of severe arthritis, and if compared with Chart 2 the marked departure from normal is at once apparent. The values range from a fasting level of 0.113 per cent. for eighteen cases to an average high point for the same number of 0.189 per cent., with many far in excess of this; three being around 0.250 per cent. at the end of the half hour and hour. In the vexed field of chronic arthritis it is sometimes difficult or impossible to differentiate sharply between severe and moderate arthritis because of the fact, on the one hand, that disability may be disproportionate to the extent or severity of the disease when important joints are involved, and, on the other hand, that severe processes affecting joints less important functionally may be tolerated easily for long periods. Furthermore, accurate classification of the types of arthritis is sometimes impossible or can be made after the lapse of time only. Thus the lowest curve on Chart 3, is probably improperly placed there and is that of a case of apparently noninflammatory bone atrophy with edema of the soft tissues. This apparent exception was maintained in repeated tests, and was reconciled with difficulty until the clinical diagnosis became apparent at a late date.

An attempt was also made to segregate arthritics into groups of severe and moderate, but for the reasons just indicated, this classifica-

21. Bang: Der Blutzucker, Wiesbaden, 1913.

tion can be only approximate. Charts 4 and 5 illustrate this attempt and show marked departures from normal in most instances. In general, it can be said that the height of the sugar curve, that is to say, the degree to which the sugar tolerance is lowered, is largely proportional to the severity of the active process per se. Severity of the process apparently plays as big a rôle as does the extent of the process in affecting the tolerance. Some of the curves on Charts 4 and 5 fall within or only slightly above normal values. In general, these excep-

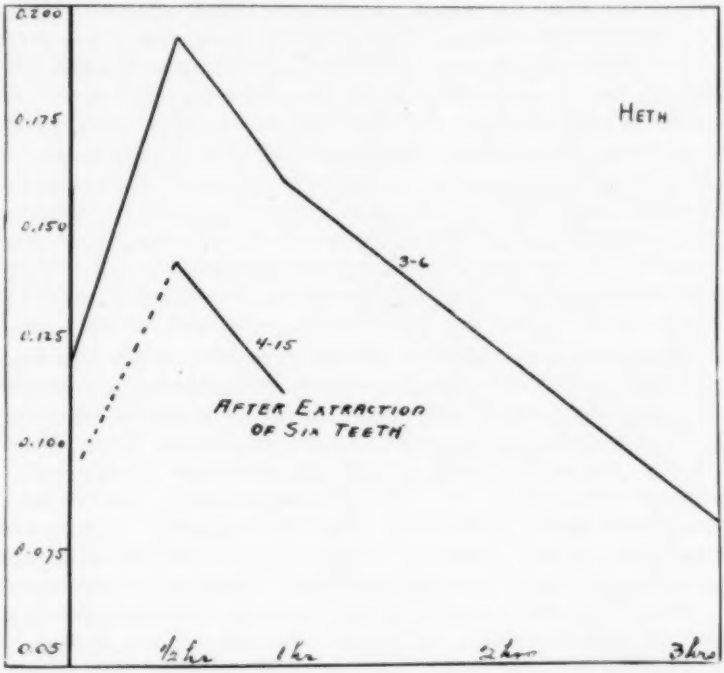

Chart 8.—The contrast in sugar tolerance of a spondylitis patient who recovered after the extraction of six teeth.

tions occur in patients who have passed the zenith of their trouble and who show a tendency to convalesce, or they occur in cases in which the distribution and severity are limited. No fixed rule exists, however, and the parallelism is not exact, although it is surprisingly close. In some apparently severe cases there is a normal or only slightly disturbed sugar tolerance. It should be borne in mind that the glucose tolerance test is merely a gross way of ascertaining deviation of a function which is probably complex and dependent on factors

not understood, and that it is not necessarily adjusted to reflect a lowered tolerance in all cases. Furthermore, as just noted, there is no absolute standard of severity of the arthritic process.

A group of twenty convalescent arthritics was then studied. These patients were representative of a severe and generally long continued arthritis, and at the time were free from symptoms. It was found that this group gave curves the average of which was importantly lower than the severe or moderate cases, falling with some exceptions (five out of nineteen cases) pretty well within long limits. That is, 74 per cent. of the group of convalescents gave a normal tolerance. It is clear, therefore, that the average curves for the moderate and mild cases can be made to vary somewhat according as the cases are classified, but by any standards the sugar tolerance tends to return to normal as convalescence proceeds. The details of certain cases in these several series will be considered later, after discussion of the field as a whole. In general, our high curves were marked more by the height to which they rose and the abruptness of the rise than by their duration at a high level, although there were some noteworthy exceptions. By and large, the higher the curve, the slower the return to normal, but it is obvious that by increasing the abscissae the curves could be made to appear flatter and indicative of a more delayed return.

On attempting to relate this disturbance to some of the other factors known to influence chronic arthritis, we conducted a series of determinations on the tolerance during the ill health and convalescence of the same individual following various procedures. It was found that there was an abrupt change in the sugar tolerance in cases which improved after removal of apparently causative foci of infection. Thus Chart 7 illustrates in a striking manner the contrast after twenty-nine days in the sugar tolerance of a soldier (Case 45) the subject of an intense arthritis of long standing in the left hip and foot, who made an abrupt and marked convalescence following tonsillectomy. The curve showing a normal tolerance was obtained fourteen days after the tonsillectomy.

Chart 8 illustrates the same thing in a man (Case 46) 40 years of age, with arthritis and tenderness of the entire spine and changes shown by the roentgen ray, who underwent marked clinical improvement after the removal of six abscessed teeth. The higher curve was obtained March 6, and the lower curve April 15.

Chart 9 shows curves representing the averages, respectively, of two tests taken during ill health, and of two during distinct convalescence in a line officer (Case 1), the subject of a widespread myositis and arthritis which had entirely incapacitated him. He had had a possible focus in a tooth removed about two months before the first curve

was obtained, and was in a stationary condition. Clinically, he made a full recovery on dietary lines alone, as described under the section dealing with dietetic measures. The two averaged curves represent an interval between them of approximately two months.

In the group of convalescents illustrated in Chart 6, it is to be noted that these soldiers convalesced in large part in the presence of demonstrable surgical foci of infection, which suggests, in the light of the proportion of cases of arthritis at large which show lowered sugar tolerance, that the disturbed tolerance may return to normal as the patient improves, even without the removal of the focal infection. At least five persons giving normal tolerance curves were the subjects of demonstrable surgical foci. As noted above, about 26 per cent. of convalescent arthritics (five in number) still gave a lowered sugar tolerance. Three of these five still had demonstrable surgical foci.

Chart 10 (Case 50) illustrates a case of chronic but mild arthritis of one knee, in an officer with a slightly lowered tolerance, who made a slow but definite improvement following repeated injections of nonspecific protein. He was apparently free from focal infection. This chart suggests, but lacking further evidences does not prove, that the lowered tolerance was restored to normal by these measures. The curves are a month apart.

Chart 11 (Case 61) represents the curves obtained during an acute febrile attack of arthritis in several joints. The highest curve was taken before treatment was instituted. The lower was obtained after the relief of symptoms by full dosage of acetylsalicylic acid. The second curve is lower than the first, but it is probable that the difference between them represents nothing more than the limitations of the method. It is clear that no important correction of the disturbed tolerance took place, though such change as did occur, was in keeping with other evidences of the tendency toward the return to normal with improvement of the arthritis. Further observations are desirable on this point. The lowest curve shows the tolerance at nearly a normal level a week after tonsillectomy, when the patient had made a complete recovery from the arthritis. The dates of the curves from above downward are respectively, April 21 and 24, and May 13.

Another experiment was conducted on the effect of acetylsalicylic acid on blood sugar, supplementing the observation made in Case 61 recorded on Chart 11. Two subjects of advanced arthritis, one improving and one stationary, were given 15 grains of acetylsalicylic acid under fasting conditions, after which the blood sugar was determined at frequent intervals, but as indicated in Table 10 there was no change in the sugar level. This is in essential agreement with the other experiment just quoted.

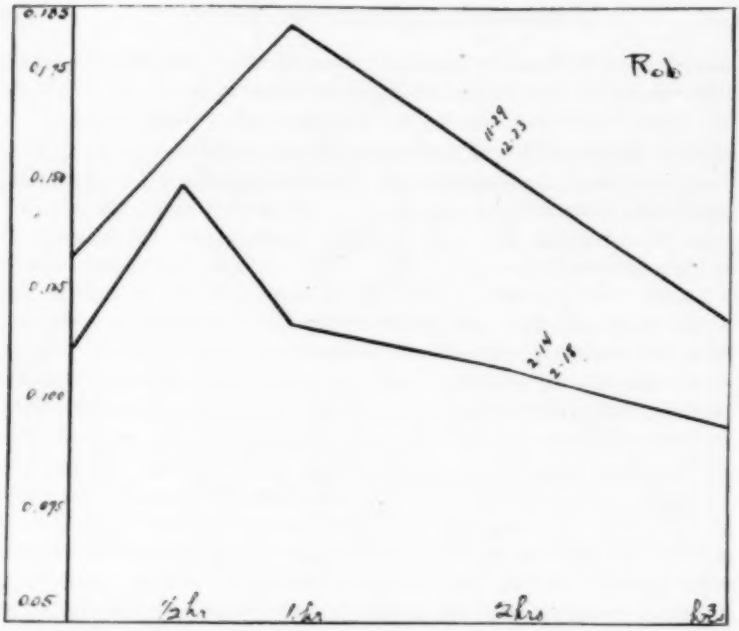

Chart 9.—The contrast in sugar tolerance before and after convalescence on a restricted diet.

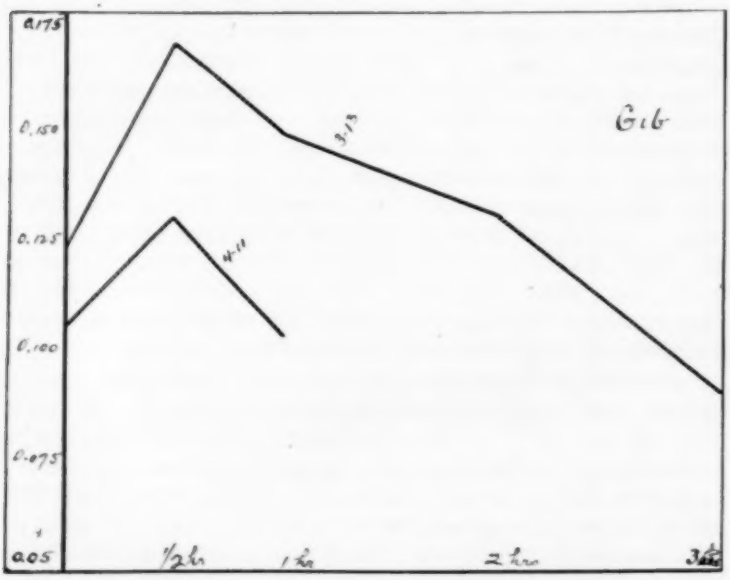

Chart 10.—The contrast before and after treatment by nonspecific protein injections.

TABLE 10.—Effect of Acetylsalicylic Acid on Blood Sugar (Feb. 22, 1919)

	Jaffy: Case 7		Lowe: Case 14	
	Blood, per Cent.	Plasma; per Cent.	Blood, per Cent.	Plasma, per Cent.
8:30	0.101	0.097	0.113	0.118
9:00	0.104	0.105	0.110	0.118
9:22 (15 grains of acetylsalicylic acid to each)				
9:50	0.106	0.110	0.110	0.110
10:20	0.106	0.110	0.106	0.112
10:50	0.109	.....	0.108	0.112
12:00	0.107	0.109	0.110	0.113

Chart 12 (Case 22) illustrates a distinctly lowered sugar tolerance in a case which made striking improvement, because of a sharp dietary, in the presence of a surgical focus. This case also will be described in detail under the section on diet. The curve next to the highest is

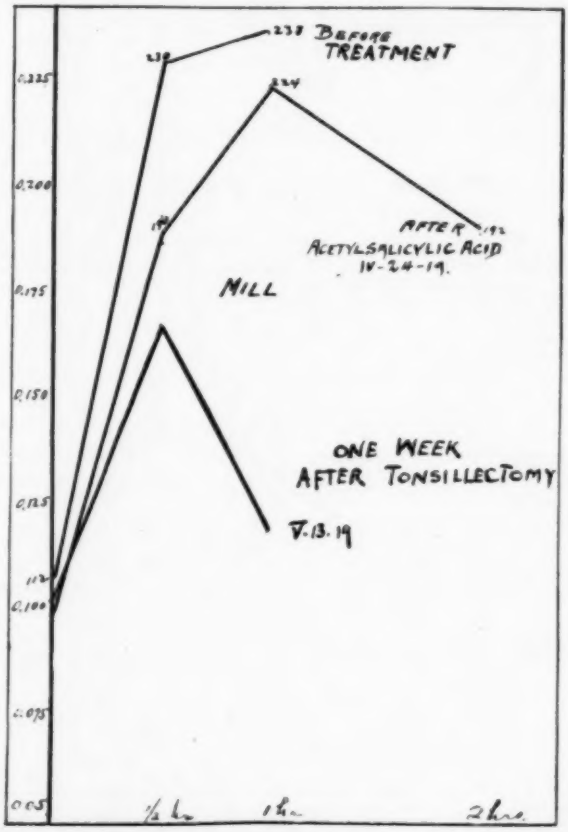

Chart 11.—The slight effect of acetylsalicylic acid and the marked effect of tonsillectomy in a severe case which recovered.

that obtained when this soldier was at the height of his trouble, which consisted in almost complete ankylosis of both hips, knees and spine, together with great limitation of function in the left shoulder. The roentgen-ray evidence was widespread and great. The third and fourth highest curves were obtained when the soldier had made an emphatic

TABLE 11.—ARTHRITICS CLASSIFIED FOR PURPOSE OF CHARTING AS FOLLOWS

Severe	Moderate	Mild
Case 6—Hayes	Case 11—Hinman	Case 17—Faulkner
4—McGrann	59—Gibson	43—Wilbert
45—Barger	3—Blower	44—Brake
46—Hetherington	12—Boyd	9—Beeman
48—Jansen	23—O'Brien	51—Lau
13—Lummis	21—Whittington	55—Cotter
15—Studebaker	32—Lt. Lynch	79—Cox
16—Bryce	53—Mrs. Kain	36—Clement (1)
10—Massood	54—Miss Anthony	
8—Martin	56—Kearly	
2—Haberle	57—Langenberger	
1—Robbins (1 and 2)	59—Flanders	
20—Wasson	47—Chaney	
14—Lowe	60—Herron	
7—Jaffy		
61—Miller		
62—McKenzie		
22—Oberg		

TABLE 12.—MEAN FASTING LEVELS FOR THE SEVERAL GROUPS

Group	No. of Cases	Blood	No. of Cases	Plasma
Normals	11	109	1	097
Convalescent arthritics	16	115	21	114
Severe arthritics	15	116	13	115
Moderate arthritics	13	112	11	110
Mild arthritics	6	115	8	121
Other pathologic types	..	...	3	118

TABLE 13.—SUGAR TOLERANCE FOR NORMALS

Name	Date	Fasting		Half Hour		One Hour		Two Hour		Three Hour	
		Blood	Plasma	Blood	Plasma	Blood	Plasma	Blood	Plasma	Plasma	Blood
Bodansky	12/27	108	...	...	...	122	...	092	...	101	
Foster	12/27	110	...	...	...	115	...	124	...	097	
Edwards	12/27	104	...	138	...	109	...	107	...	099	
Jones	1/ 3	101	...	147	...	147	...	115	...	098	
Smith	1/ 3	111	...	158	...	104	...	094	...	083	
Hudson	3/14	108									
Edder	3/14	100									
Meador	12/28	112	...	...	...	127	...	115	...	115	
Carter	1/29	128	...	138	136	114	100	096	088	098	088
Cutshall	12/28	122	...	...	...	125	...	114	...	083	
Monahan	.....	097	097	120	122	094	088				
Mean of 9	.....	109	...	140	...	117	...	107	...	097	

* In order to save space, the tables showing the presence or absence of glycosuria for each of the periods in the following tests are omitted. The threshold value fell between 0.170 and 0.180.

TABLE 14.—Sugar Tolerance for Arthritics

Name	Date	Fasting		Half Hour		One Hour		Two Hour		Three Hour		
		Blood	Plasma	Blood	Plasma	Blood	Plasma	Blood	Plasma	Blood	Plasma	
Blower	12/10*	...	127	...	...	...	188	...	135	...	143	
Beeman	12/26	123	...	...	...	175	...	109	...	110		
Boyd	1/ 9	119	...	160	...	165	...	146	...	108		
Lummis	1/ 9	107	...	179	...	123	...	100	...	081		
Studebaker	1/16	144	...	221	...	192	...	161	...	152		
Bryce	1/16	150	...	212	...	250	...	200				
Massood	12/31	208	...	...	...	262	...	212	...	167		Omitted from aver.
	1/ 2	124										
	1/ 6	144	...	168	...	220	...	188	...	113		
Martin	12/22*	...	161	...	...	...	166	...	156	147		
	12/26	120	...	175	...	125	...	125				
	3/ 5	106	109	198	208	186	204	185	188	186	185	
Haberle	12/10*	...	150	...	...	...	150	...	150	...	150	
	1/17	...	100	...	120	...	139	...	120	...	091	
	3/ 7	102										
O'Brien	2/ 4	120	...	175	175	147	133	114	107	080	068	
Robbins	11/29*	...	125	...	...	...	188	...	167	...	107	
	12/23*	...	142	...	...	...	185	...	140	...	134	
	12/30	109										
	2/14	107	110	130	132	117	120	107	104	098	088	Entered on "convalescent" also
	2/18	118	115	169	167	120	115	118	111	110	108	
	4/11	106	106	134	136	094	091	...	...	...	...	After exercise
Wittington	1/31	...	110	...	161	...	123	...	106	100		
	2/ 4	123	123	178	190	131	126	115	108	091	086	
Wasson	1/29	117	115	181	181	139	136	...	136			
	3/ 8	094	100	150	153	144	144	100	100	115	115	
Lowe	1/13	146	...	250	...	177	...	120	...	074		
	2/22	113	118									
	5/11	108	108	200	214	167	163					
Jaffy	12/11*	...	107	...	...	...	246	...	181	...	133	
	2/22	101	097									
	3/ 7	109										
Faulkner	1/22	128	122	130	135	140	144	...	112	090	075	
Hayes	12/11*	136	...	...	...	...	178	...	121	...	079	
	12/26	123										
	2/ 6	...	135									
	2/17	133	132	195	201	250	250	175	173	101	088	
	5/ 9	109	108	179	182	185	192					
McGrann	12/10*	...	097	...	...	...	231	...	172	...	107	
	2/ 7	102										
Oberg	1/31	...	097	...	182	...	160	...	101	...	089	
	2/ 4	114	106	238	246	214	239	206	208	067	064	
	3/ 2	098	094	214	238	278	294	312	326	259	266	After fasting
	3/14	102	103	169	169	187	180	200	197	071	063	
	4/25	112	108	181	185	200	208	156	140	...	...	Just before tonsillectomy
	5/ 8	115	112	150	158	100	096	...	...	...	...	A week after tonsillectomy
Hinman	12/ 2	185										
	1/ 6	123	...	203	...	125	...	102	...	075		
Wilbert	2/21	129	115	162	170	158	158	107	107	101	100	
Brake	2/21	125	130	152	156	131	129	125	121	120		
Barger	2/27	104	100	179	190	182	186	177	181	084	...	Before tonsillecto'y
	3/28	103	103	128	130	110	111	101	100	091	...	After tonsillectomy
Hetherington	3/ 5	122	124									
	3/ 6	115	120	188	195	169	167	...	...	081	083	
	4/15	...	...	141	143	114	113	...	...	...	...	Six teeth out about 4 weeks ago
Jansen	3/ 6	115	117	177	181	158	174	095	095			
Gibson	3/13	125	125	173	171	155	150	144	131	094	091	
	4/11	105	107	127	131	107	104	...	...	...	...	Protein injection 5 days ago, feels better now
Lau	3/22	085	086	098	100	096	099	081	082	087	088	
Lt. Lynch	3/22	100	100	118	120	120	...	096	095	090	090	
Mrs. Kain	3/22	099	098	188	190	116	120	072	065	065	065	
Miss Anthony	3/26	099	...	174	...	172	...	150	...	125		
Cotter	4/ 2	110	108	128	129	116	118	088	086	075	070	
Kearly	4/ 6	115	117	153	161	099	091	080	081			
Langenberger	4/15	111	111	172	180	100	094					
Bruno	4/16	121	123	169	171	156	150	...	...	...	...	Also on convalescent sheet
(after exercise)	4/19	112	111	138	140	111	111	105	...	...	...	
Flanders	4/19	108	107	154	163	155	155					
Cox	4/19	128										
Chaney	4/20	108	108	135	141	160	165	135	130			
	3/ 6	102	103	158	160	137	137	114	123	100	101	
Herron	4/20	104	105	188	205	131	121	100	096			
Miller	4/21	107	112	224	230	238	238	...	...	...	...	Before aspirin
	4/24	097	100	188	190	214	224	197	192	...	...	Symptoms relieved by aspirin
	5/13	104	103	165	122	119	...	...	...	...	...	A week after tonsillectomy
	4/28	115	115									
Lord	5/11	108	107	188	194	163	163	...	...	...	...	Arthritis, empyema, febrile (101 F.)
Folden	5/18	110	110	210	218							
McKenzie	4/29	...	132	...	215	...	188	...	...	...	...	Febrile, 100/2, no aspirin

* The analyses in the cases marked with an asterisk were made under the direction of Miss M. B. Wishart, who was associated with Capt. F. M. Allen on the diabetic service of the hospital. The writers desire to express their obligation for this and other courtesies.

therapeutic advance following diet. The lowest curve represents the return of the sugar tolerance to practically normal limits, following the removal of a necrotic pair of tonsils, after he was well on in convalescence and able to walk with crutches.

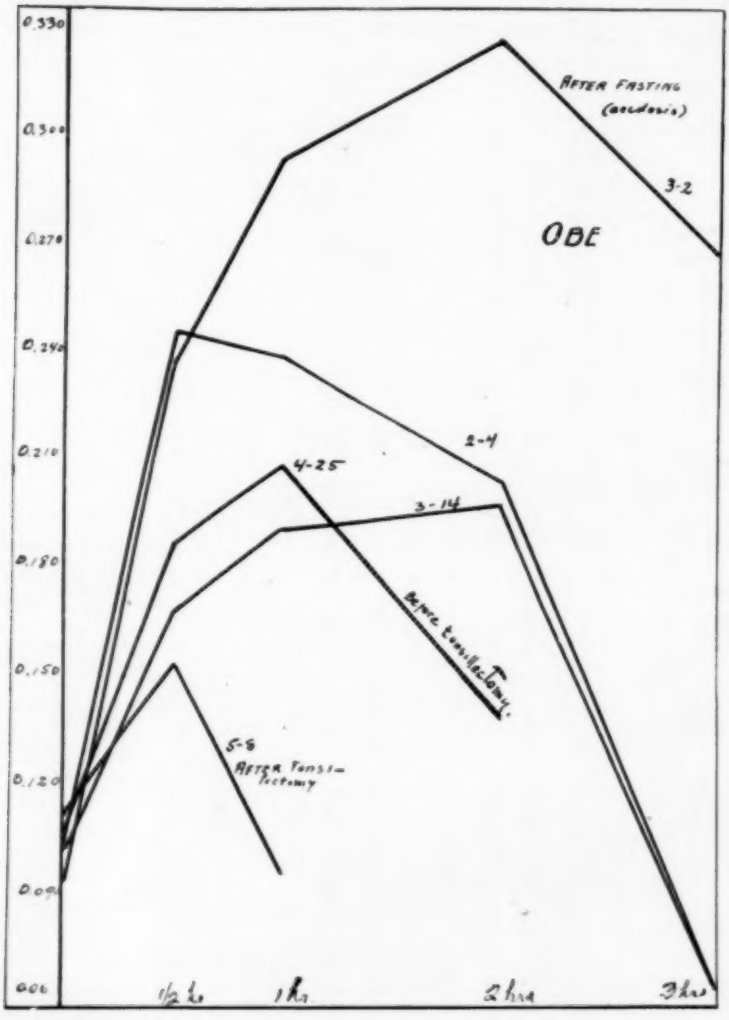

Chart 12.—The lower four curves show the tendency of a lowered tolerance to return to normal following improvement under diet and, later, tonsillectomy (see text for details).

Therefore it seems clear that as cases of arthritis improve, irrespective of the therapeutic measure to which this is due, the lowered sugar tolerance tends strongly to a return to normal. It seems to do so most rapidly, however, after surgical removal of the causative infection.

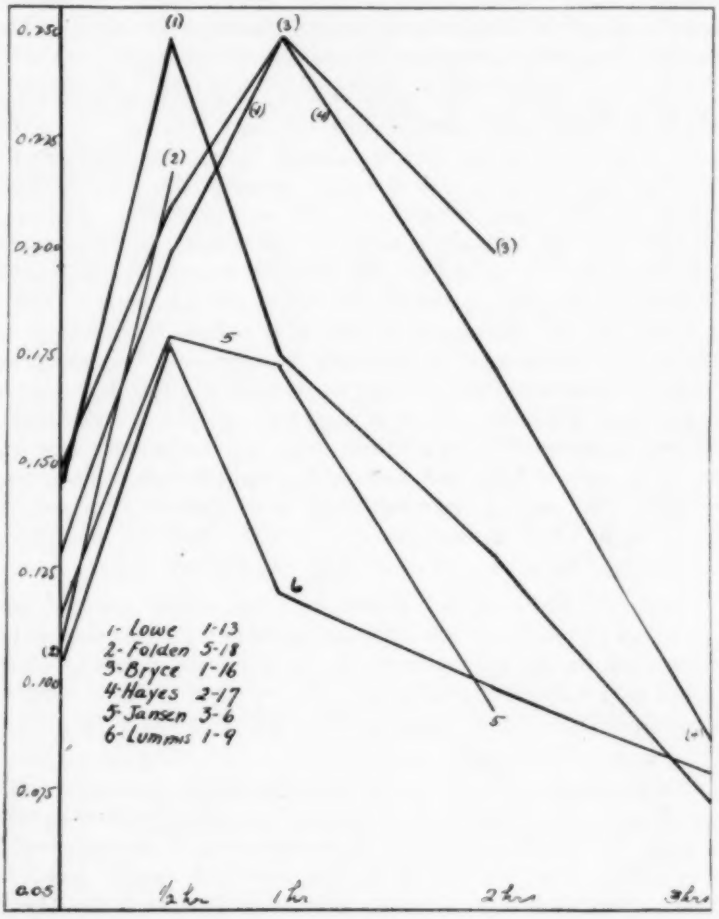

Chart 13.—The persistence of lowered sugar tolerance in chronic cases from which all demonstrable foci of infection had been removed.

Our experience suggests that the sugar tolerance test may sometimes be helpful to indicate whether all foci have been removed. For example, a case of active arthritis of moderate chronicity may fail to

improve after the removal of dental foci. If the tonsils in such a case are apparently normal, as often happens, the maintenance of a definitely lowered sugar tolerance would suggest that foci are still operative and presumably in these tissues. Other applications are obvious and may later be justifiable, but at present there are too many variables to warrant much emphasis, except within narrow limits. It must be borne in mind that long standing cases from which all demonstrable foci have been removed may retain their lowered tolerance.

Chart 13 represents high curves obtained in a series of cases from which all demonstrable surgical foci had been removed. It is, of course, impossible to say that any person is free from a focus of infection, and it may be that the high curves of this chart indicate greatly lowered sugar tolerance referable to hidden foci. The presumptive evidence, however, is to the opposite effect, especially as it is well recognized that in long standing cases the removal of foci may be followed by less gratifying results, or failure, and it is, perhaps, easier to believe that the persons in question have suffered a dislocation of physiologic function which persists after the removal, or is independent, of focal infection. Thus the high single peak occurred in a soldier (Lowe, Case 14) who had been ill more than two years, who had had his tonsils removed months before, who had no pathology in his mouth or genito-urinary tract, and who had had attention to his sinuses as well. This case was very refractory to all kinds of treatment, of which he had had thirteen different varieties, including nonspecific protein injection, a brief period of diets and hydrotherapy.

Curve 3 (Br., Case 16) is that of a civilian, 45 years of age, studied by permission of the commanding officer. He had been under observation for about four years, for the first year or two of which he had been examined and treated from every angle for the removal of focal infections. Failing relief by all these methods, he made a gratifying improvement, which amounted to recovery, along dietary lines. Curve 4 (Hayes; Case 6) is that of another regular army man who had been ill about two years. He had been treated at Hot Springs and had had his tonsils removed four or five months previous to this observation, having at the time no other detectable surgical infection. This patient made a 50 per cent. advance under dietary procedures, and finally made a complete symptomatic recovery by the continuation of these measures, supplemented by potassium iodid, sweats and cod liver oil.

Curve 5 (Jansen; Case 48) was afforded by a case of vertebral arthritis. The patient had had a tonsillectomy three months before,

and was making a substantial improvement in the absence of other demonstrable foci in the mouth or genito-urinary tract. This case was of much clinical interest. (For details, see section on "Clinical Considerations.")

Curve 6 (Lum., Case 13) is that of a woman, 42 years of age, studied by permission of the commanding officer, who had been exhaustively examined and treated for foci to the point of removing her appendix, and an operation for gallstones, which latter proved unnecessary. She was at this time suffering from a subacute arthritis.[21a] As a routine measure, and in the absence of any detectable pathology,

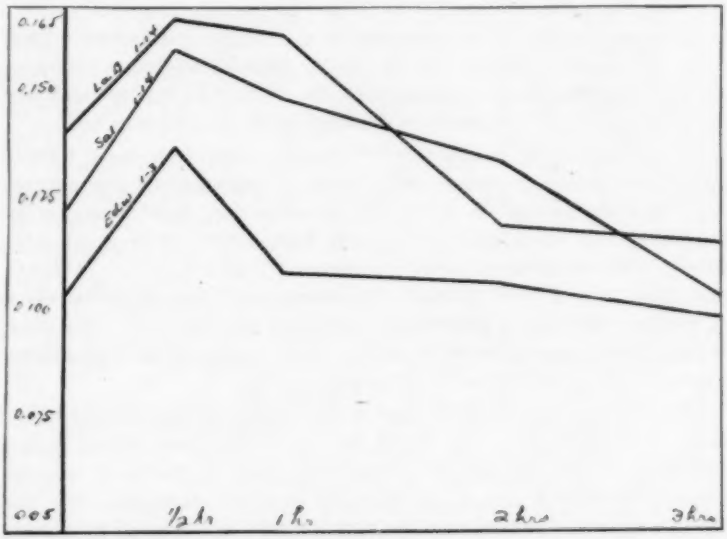

Chart 14.—Normal and slightly lowered sugar tolerance in normal men with enlarged tonsils but no systemic symptoms.

her tonsils were removed June, 1919. They proved negative for *Streptococcus hemolyticus,* were very small and were apparently not potential or actual foci of infection. She was still sick in February, 1920.

Case 57 (Langenberger) is another example of the same condition, not charted here, and others could be cited.

21ª. This patient kept her symptoms more or less modified by a low dietary, which she was led to adopt largely by her own experience. This diet was shown later to average about 2,000 calories. The beneficial effect of a very low diet or starvation on her symptoms had been repeatedly demonstrated and it is planned to report this case in greater detail later.

Chart 16 shows the curves obtained from three supposedly healthy persons, the subjects of marked tonsillar pathology without symptoms. One curve was very slightly elevated above the normal, and the other two fell within normal limits. One of these patients showed such gross pathology that his tonsils were removed a day or two later as a prophylactic measure. The significance of this chart is further borne out by the curves in the convalescent arthritics, three of whom were the subject of demonstrable surgical foci and yet showed a normal tolerance.

It is important, therefore, to note that, by and large, the disturbance of the sugar tolerance, as here considered, due to focal infection, apparently accompanies the failure of the organism successfully to maintain its wall of defense and is apparently restored to normal when this defense returns. In this light a lowered tolerance, following on a focus, becomes an intermediary, or, at least, a concomitant step in the pathology of arthritis and possibly other conditions as well.

In the course of conducting 109 complete sugar tolerance tests, a number of points developed which were of considerable interest, but could not be carried to their full development, partly because of the closure of the hospital and partly because of the press of other work. One of these occurred in connection with Case 22 (Oberg), described fully under "Dietary Considerations," the sugar tolerance at various times being graphically portrayed on Chart 12. This chart is drawn to a scale different from the others owing to the impossibility otherwise of including on it the uppermost curve.

In the course of the treatment of this soldier he was subjected to a sharp fast, amounting practically to starvation, which lasted during February 27, 28, and March 1, and until noon of March 2. On the morning of March 2, a sugar tolerance test was conducted. At that time he showed a moderate starvation acidosis, as indicated by acetone bodies in the blood plasma and urine, and a blood carbon dioxid of slightly under 50 volumes per cent. Reference to the chart shows that although the fasting blood sugar was at about the previous level, he showed a very marked intolerance to the ingested glucose, the curve rising to about 0.325 per cent. at the end of the second hour, being still greatly elevated at the end of the third hour. One other case illustrative of the same phenomenon has come to our attention, and it appears that the condition of acidosis may be accompanied by a greatly lowered sugar tolerance, or may at least further depress an existing low tolerance. This point is worthy of further attention. March 14, when his acidosis had been relieved by feeding carbohydrate, the sugar tolerance fell markedly to a point distinctly lower than it had been at any time previously, the highest point on the curve being 0.198 per cent.

TABLE 15.—Sugar Tolerance for Arthritics

Name	Date	Fasting		Half Hour		One Hour		Two Hour		Three Hour	
		Blood	Plasma	Blood	Plasma	Blood	Plasma	Blood	Plasma	Blood	Plasma
Eckman	2/ 9	100	097	168	183	159	160	111	107	113	101
Moseley	2/ 9	095	097	111	113	107	100	084	079	083	079
Black	2/ 9	121	119	190	188	174	168	115	102	088	074
Stone	2/10	109	108	150	...	140	137	092	091	080	081
Collins	2/10	120	...	171	...	126	123	114	108	110	100
Stewart	2/10	103	099	188	193	135	139	097	095	102	096
	2/17	...	119	...	147	...	117	...	112	...	112
(after exercise)	2/18	...	150	...	230	...	210	...	165		
Cullen	2/12	100	097	182	197	135	131	140	080	080	075
	2/17	...	130	...	195	...	155	...	120	...	088
(after exercise)	2/18	...	119	...	143	...	248	...	197		
Moehler	2/11	...	125	...	138	...	131	...	079	...	110
Moon	2/11	...	114	...	148	...	124	...	091	...	100
Gaffney	2/12	110	107	152	150	...	122	097	081	...	097
Cabbage	2/12	113	107	143	144	131	125	088	083	088	088
Robbins	2/14	107	110	130	132	117	120	107	104	093	088
	2/18	118	115	169	167	120	115	118	114	110	102
Tally	2/19	...	120	...	125	...	133	...	090	...	107
Morris	2/19	110	106	144	144	117	115	101	099		
Thompson	2/19	115	120	100	108	133	130	088	082	092	087
Gross	2/20	...	121	...	126	...	115	...	119	...	109
Greenberg	2/20	128	120	145	150	155	156	100	100	100	100
Kerr	2/20	139	131	137	144	143	131	125	121	125	080
Clement	3/20	...	...	225	230						
Bruno	4/16	121	123	169	171	156	150				
(after exercise)	4/17	111	112	138	140	111	111				
Mean of all but those after exercise		115	114	154	154	140	135	110	106	100	095

TABLE 16.—Sugar Tolerance for Other Pathologic Conditions

Name	Date	Fasting		Half Hour		Oue Hour		Two Hour		Three Hour		
		Blood	Plasma	Blood	Plasma	Blood	Plasma	Blood	Plasma	Blood	Plasma	
LaBoyteaux	1/14	142	...	167	...	163	...	120	...	116	...	Tonsils
Salvatore	1/14	124	...	160	...	149	...	134	...	103	...	Tonsils
Meador	1/14	131	...	185	...	153	...	167	...	108	...	Frontal sinus
Fountain	1/18	143	...	206	...	155	...	111	...	104	...	Plumbism
Campbell	1/18	136	...	188	...	132	...	094	...	093	...	Gas bronchitis
Harris	1/18	107	...	150	...	171	...	116	...	075	...	Amebic dysentery
King	1/18	125	...	162	...	155	...	105	...	100	...	T.B. peritonitis
Muse	1/23	147	...	234	...	185	...	172	...	153	...	T.B. bones and joints
Fauts	1/26	...	121	...	152	...	121	...	108	...	098	Fractured spine
Frogley	2/ 6	...	136	...	147	...	158	...	122	...	...	T.B. pleurisy
Smith	2/ 7	100	102	153	158	130	124	120	116	111	108	
Hampton	3/21	100	...	125	...	129	...	108	...	084		
Mean of 10	.....	124*	118	176	148	157	138	120	114	102	099	

* This figure for the fasting level of the whole blood is too high. The value for the plasma of the fasting blood is more nearly correct.

There is in this observation an apparent incompatibility between the relief of symptoms, accompanied eventually by a lowered sugar curve, following a reduced ingestion of carbohydrate, on the one hand, and the greatly heightened curve consequent upon complete starvation on the other hand. This discrepancy is more apparent than real, how-

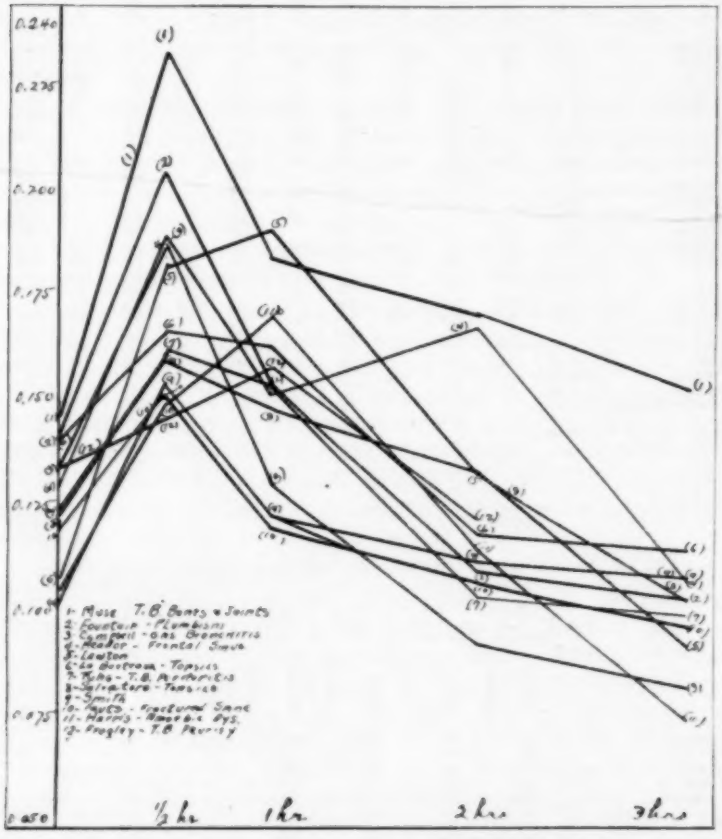

Chart 15.—The sugar tolerance in miscellaneous pathologic cases.

ever, as the condition of starvation induces an added pathology of its own and otherwise modifies normal physiologic processes.[21b]

A lowered sugar tolerance is specific for no disease and has been noted in a variety of conditions. It has been regarded, however, as more or less peculiar to certain conditions and definitely characteristic

21b. It is planned to discuss this point more fully at a later date.

of some of them. It is important that there be recorded the results of sugar tolerance tests in as many different diseases as possible, and there were, therefore, included in the present study determinations of the sugar tolerance in twelve cases of miscellaneous diseases at large, as they presented at the hospital.

Reference to Chart 15 will show the studies and the results of the test in each case. The highest curve is that afforded by a colored man Case 18 (Muse), with widespread tuberculosis of the periosteum of the long bones, of the phalanges and of joints of the hands and feet. It is a moot point whether this case does not belong as much in the group of arthritics as elsewhere, since he also had secondary infection of the exposed and denuded bony surfaces.

The next highest curve is that in a case of chronic lead poisoning with the marked atrophy characteristic of that condition. The next highest curve was that of an officer alleged to have arthritis, accompanied by mild neurasthenia, and was accidently included on this chart. It is rather noteworthy that Curve 7 and Curve 12 were afforded by cases of tuberculous peritonitis and tuberculous pleurisy, respectively, the former being only slightly elevated, and the latter well within normal limits. The case of tuberculous peritonitis was in a satisfactory condition of stability, but the case of pleurisy, in an army nurse, showed a large effusion in one pleural cavity. The diagnoses of the other conditions are noted on the curves.

Chart 16 is designed to illustrate the relative positions of the mean curves obtained from the various groups of cases studied. Reference to it shows that the severe arthritics gave the highest curves, the miscellaneous pathologic cases the next highest and moderate arthritics the next; the mild and convalescent arthritics followed with curves of about the same height; the curves in the normal cases being the lowest of all. It is to be noted that the miscellaneous pathologic cases were studied and recorded as they became available, and that the composite curve for them fell by chance in the position indicated. It is probable that selection could be made of certain types of miscellaneous pathologic cases which would determine such a composite curve at either a higher or a lower level according to the groups chosen.

It has generally been believed, as Hamman and Hirschman[16] point out, that, with the exception of disease of the pancreas, disturbances of the thyroid are the most common cause of altered carbohydrate tolerance. These authors emphasize, however, that even in hypothyroidism, sugar tolerance shows perplexing combinations, although in a general way low in hyperthyroidism, and abnormally high in hypothyroidism and that individual patients display wide latitude in their responses. The same conditions obtain in connection with disturbances

of the hypophysis, where similar individual discrepancies occur. Again, it has long been known that in nephritis the blood sugar is often unusually high. However, as Hamman and Hirschman remark: "It is not always high; sometimes it is at the normal level, and why some cases have hyperglycemia and others have not, has never been satisfactorily explained."

It would seem, however, in the light of the evidence herewith adduced, that lowering of the sugar tolerance, as exemplified by the glucose tolerance test, rests, in part at least, on somewhat more fundamental pathologic processes than has hitherto been suspected. It seems to stand in some relation to inflammatory processes at large, and it appears from the data adduced herewith, that the incidence of an inflammatory process in a healthy person may induce a lowered sugar tolerance, that is a high curve.[22] There can be here instanced the case of Meador, a normal man, before and after the onset of frontal sinusitis. As seen by referring to Chart 2, illustrating the sugar tolerance of normal individuals, he there gave a curve (No. 8, Dec. 28, 1918), which rose only to 0.127 per cent. at the end of the first hour, and later when he was the subject of an acute inflammatory process, he gave a curve[23] which was at 0.190 per cent. at the end of one-half hour, at 0.152 per cent. at the end of the first hour and at 0.167 per cent. at the end of the second hour. On the other hand, other curves here adduced definitely prove that a lowered sugar tolerance of marked degree may abruptly return to normal after the removal of a focus of infection. This is illustrated in four cases of this series[24] in such a striking way as to be unquestionable.

It is entirely possible that some departures from normal observed in studying nephritis and thyroid and hypophyseal disorders, etc., are referable to such agencies as focal infections, and that we may really be determining under these circumstances the lowered tolerance due to them rather than to the disease primarily under consideration.

This applies, of course, to the miscellaneous diseases we have studied and recorded on Chart 15, and suggested the inexpediency of extending such observations unless carefully controlled. Thus the high curve (2) afforded by the case of plumbism, for example, may have been due to a focus which we did not at that time search for or suspect as having any bearing on the result.

It would seem important, therefore, in studying the carbohydrate tolerance of any disease in a given individual, to make sure that there is no focus in the field operating to alter the reaction to the glucose tolerance test.

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22. A high level of blood sugar in furunculosis has been noted by Gettler and St. George, J. A. M. A. **71**:2033 (Dec. 21) 1918.

23. Chart 15, miscellaneous pathologic cases, Curve 4, Jan. 4, 1919.

24. Charts 7, 8, 11 and 12.

Finally, there is called prominently into the foreground the possibility that other diseases, of which a lowered sugar tolerance is a recognized symptom, may originally owe their characteristic feature of a lowered tolerance to such factors as causative agents.

A lowered sugar tolerance, as measured by the glucose tolerance test, seems to be a more common occurrence than has been appreciated. In view of the demonstrated relation of focal infection to sugar tolerance; in view of the frequency of foci in arthritis and at large; in view of the frequency of arthritis as a disease and the frequency

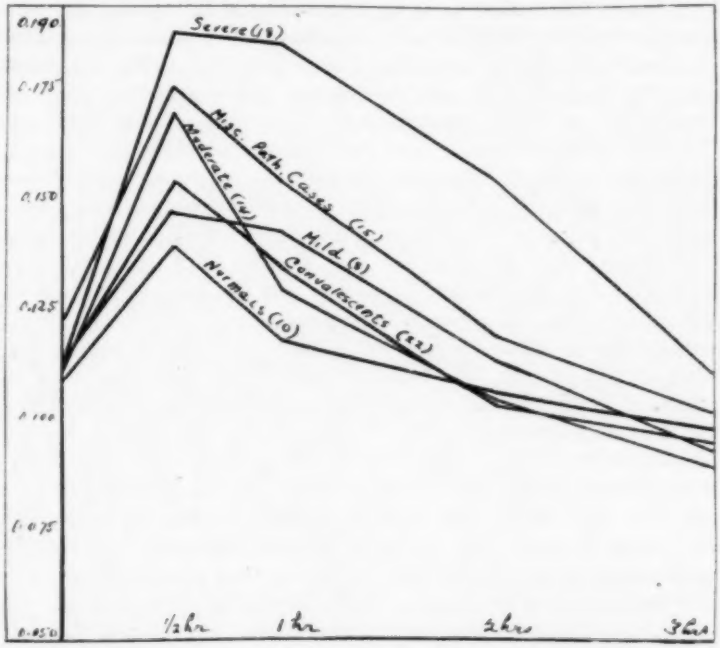

Chart 16.—The average curves for the several groups of severe, moderate, mild and convalescent arthritics, miscellaneous pathologic cases and normals.

with which it is accompanied by a lowered sugar tolerance, it seems necessary to modify the view which ascribes to disturbance of thyroid function, next to disease of the pancreas, the most common cause of altered carbohydrate tolerance as measured by this test. The thyroid or other glands may be involved in the chain starting with focal infection, but the glucose tolerance test reflects, of course, only a part of the carbohydrate metabolism as a whole, and it is unprofitable in view of our incomplete knowledge to speculate much as to its full signifi-

cance. It is clear, however, that most arthritic patients are unable to remove from the circulating blood, as does a normal individual, the carbohydrate which reaches it from the gastro-intestinal tract.[25]

Hamman and Hirschman cite one case of rheumatic fever with afternoon temperature as high as 101 F., in which there only occurred a very slight rise of blood sugar after taking 100 gm. of glucose. Opportunity has permitted us to study only a few cases of febrile "inflammatory rheumatism," but the three cases which we observed showed a markedly lowered tolerance. One of these has been recorded on Chart 11, giving two markedly elevated curves during the course of an acute febrile arthritis before and during symptomatic control of symptoms by acetylsalicylic acid. Another case is illustrated on Chart 13 (Curve 2; Folden; Case 63). The patient was at that time apparently free from demonstrable surgical foci and was in the middle of a widespread rheumatic exacerbation. This case is described under "Clinical Considerations." The third patient (McKensie; Case 62), during an attack of diffuse febrile arthritis with temperature up to 100.4 F. at the time of the test, gave a lowered tolerance with a curve up to 0.215 per cent. This curve is not charted, the figures for plasma sugar being: 10 a. m., 0.132 per cent. fasting; 10:30 a. m., 0.215 per cent. after 100 gm. glucose; 11 a. m., 0.188 per cent. This case was interesting in that the patient had had previous attacks of considerable severity, during which he received as many as eleven or twelve injections of phylacogens, one injection daily. On admission from the command to the hospital, he had been sick and febrile for three days, and had had three injections of phylacogens, obtained on his own responsibility outside. These were discontinued, and several days later the temperature fell to normal under routine treatment. About ten days later, during a sick leave, he again became ill in the same way, being admitted with diffuse tenderness and fever. He had had no phylacogens on this occasion. It was at this time, April 29, 1919, that the above test was made. This man had a dental abscess. The tonsils and genito-urinary tract were reported normal, and he had a four plus Wassermann.

25. The propriety of withholding large amounts of carbohydrate from some such cases finds ample corroboration in the restricted diets discussed in Part V. It is suggested that this principle may also have application to some other conditions accompanied by this disturbance, in the effort to spare an obviously weakened function.

(Parts IV and V will be published in the April issue.)

A METHOD OF ANALYZING THE ELECTRO-CARDIOGRAM *

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The electrocardiogram as generally taken consists of three leads, obtained by using the two arms and the left leg as the contact or leading off points. Einthoven[1] has shown that these three leads bear a definite mathematical relationship to one another and has used an equilateral triangle to express this relationship graphically. For the better understanding of the succeeding parts of this paper we shall consider this mathematical relationship and its graphic representation at some length.

The mathematical relationship is expressed by the equation: lead II equals lead III plus lead I. This means that the height of the ordinate in lead II of the electrocardiogram at any instant is the sum of the heights of the ordinates in leads III and I. The reason for this relationship can be appreciated if we consider the string galvanometer simply as an instrument for measuring differences of potential.[2] If now we wish to measure the difference of potential between the right arm and the left leg (lead II) at any instant, we can do it either directly by connecting the galvanometer with the right arm and left leg (lead II) or indirectly by taking some other point, as for example the left arm, finding the difference of potential between the right arm and the left arm (lead I) and between the left arm and the left leg (lead III) and adding them together. In a similar manner, if one wishes to find the difference in elevation (potential) between two towns, A and B, one may either subtract the elevation of A from the elevation of B (lead II), or one may take a third town, C, find the difference in elevation between A and C (lead I) and between B and C (lead III) and add them together. It is clear that the answer must be the same whichever way one proceeds. Thus, if the E. K. G. gives us a true record of differences of potential, it must follow that for

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1. Einthoven, W.: The Different Forms of the Human Electrocardiogram and Their Signification, Lancet **1**:853, 1912.

2. The string galvanometer, because of the fact that the resistance of its circuit is not infinite, has a slight tendency to decrease the difference of potential between the leading off points, but ordinarily the error from this source is negligible, and the mathematical relationship between leads holds within the limits of experimental error.

any and every moment during the cardiac cycle lead II equals lead III plus lead I; or, as it is more convenient for practical purposes to put it, lead II minus lead I equals lead III.

To express this relation graphically Einthoven[1, 3] makes use of an equilateral triangle. The peculiar fitness of the equilateral triangle is due to the fact that the projections on the sides of an equilateral triangle of any straight line drawn within the triangle have a relationship similar to the relationship between the leads of an electrocardiogram. Figure 1 will demonstrate this point.

O A is any straight line drawn within the equilateral triangle R L F. The projections of O A on the three sides correspond to the three leads of the electrocardiogram and are labeled ϵ_1, ϵ_2 and ϵ_3, respectively. The geometrical proof given shows that $\epsilon_2 = \epsilon_3 + \epsilon_1$. This equation will hold whatever be the position of O A, provided we give ϵ_1, ϵ_2 and ϵ_3 negative values when they would have negative values in the electrocardiogram.

Since Einthoven first demonstrated these mathematical and geometrical relationships, numerous investigators[4] have made use of them in analyzing electrocardiograms. The methods used have been various minor modifications of the original method of Einthoven, Fahr and de Waart,[3] which consists in finding the values of the three leads at any chosen instant and in substituting these values in certain formulas, thereby obtaining a linear value called "E" or the "manifest value," and an angular value, "α." These two values determine the length and direction of a vector which corresponds to the line O A in Figure 1; O A in Einthoven's formula having the linear value E, and the angle C A O being α. The length, E, of the vector gives the manifest value of the potential difference as shown by the three leads, but the vector as drawn by Einthoven in his original paper,[1] and thereafter by numerous users of this method[3, 4] is in a direction directly away from the point at which the center of negativity is located.

Carter, Richter and Greene[5] have developed an interesting modification of Einthoven's method. By means of an equilateral triangle,

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3. Einthoven, W., Fahr, G., and deWaart, A.: Ueber die Richtung und die manifeste Grösse der Potentialschwankungen im menschlichen Herzen und über den Einfluss der Herzlage auf die Form des Elektrokardiogramms, Arch. f. d. ges. Physiol. **150**:275, 1913.

4. Pardee, H. E. B.: Form of the Electrocardiogram, J. A. M. A. **62**:1311 (April 25) 1914. Fahr, G.: Simultaneous Records of Heart Sounds and the Electrocardiogram, Heart **4**:147, 1912.

5. Carter, E. P.; Richter, C. P., and Greene, C. H.: A Graphic Application of the Principle of the Equilateral Triangle for Determining the Direction of the Electrical Axis of the Heart in the Human Electrocardiogram, Bull. Johns Hopkins Hosp. **30**:162 (June) 1919.

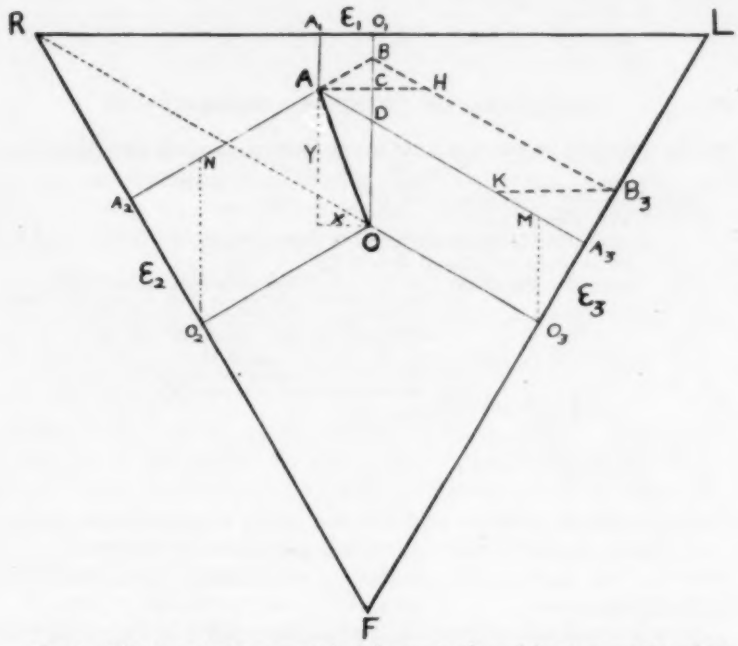

Fig. 1.—This is a simple geometrical demonstration of those properties which make the equilateral triangle peculiarly suitable for use in analysis of electrocardiograms.

The values of the rectangular coordinates (X, Y) of a point (A) are found algebraically in terms of the three leads (e_1, e_2 and e_3).

PROPOSITION: The longest projection on the sides of an equilateral triangle of any straight line drawn within an equilateral triangle equals the sum of the projections on the other two sides.

LET A O* be any straight line drawn within the equilateral triangle R L F. Let e_1, e_2, and e_3 be the projections of A O on the three sides of the triangle, obtained by dropping perpendiculars (AA_1, AA_2, AA_3, OO_1, OO_2, OO_3) from the ends of the line A O upon the sides of the triangle.

TO PROVE THAT $e_2 = e_3 + e_1$.

CONSTRUCTION:

1. Produce A_2A until it meets OO_1 at B.
2. Draw BB_3 perpendicular to L F.
3. Draw A H parallel to R L cutting B O at C.
4. Draw K B_3 parallel to A H.
5. Draw R O_3* the perpendicular bisector of L F.

PROOF

$A_2O_2 = B_3O_3$ for they are the projections of OB and the projections on the sides of an isosceles triangle of any line perpendicular to the base are equal.

$A_2O_2 = A_3O_3 + A_3B_3$ for $B_3O_3 = A_3O_3 + A_3B_3$.

$e_2 = e_3 + A_3B_3$ for $A_2O_2 = e_2$ and $A_3O_3 = e_3$.

$= e_3 + \frac{1}{2}K\,B_3$ for $A_3B_3 = \frac{1}{2}KB_3$ because triangle K A_3B_3 is similar to triangle R L O_3 and L $O_3 = \frac{1}{2}$ R L since F L = R L and L $O_3 = \frac{1}{2}$ F L.

$= e_3 + \frac{1}{2}A\,H$ for K B_3 = A H because parallel lines included between parallel lines are equal.

$= e_3 + A\,C$ for $\frac{1}{2}$ A H = A C because A C = C H since triangle A B C = triangle H B C (The two triangles have the common side B C, angle A C B = angle H C B = a right angle, and angle A B C = angle H B C = 60° since perpendiculars to the sides of an equilateral triangle intersect at angles of 60°.)

$e_2 = e_3 + e_1$ for A C = e_1, because parallel lines included between parallel lines are equal.

Q. E. D.

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* In the figure the point O has been made the center of the triangle for the sake of simplicity in construction but the proof does not depend on this fact and will hold whatever be the position of the line O A. As a matter of fact the point O is taken at the center of the triangle in the subsequent part of this paper.

TO FIND THE VALUE OF THE RECTANGULAR COORDINATES (X, Y) OF THE POINT A IN TERMS OF e_1, e_2, AND e_3

Draw NO_2 and MO_3 parallel to OO_1

Then $X = A\ C = A_1O_1 = e_1$

$$Y = C\ O = (B\ O - B\ C) = (D\ O + D\ C)$$

$$= \tfrac{1}{2}\ (B\ O - B\ C + D\ O + D\ C)$$

$$= \tfrac{1}{2}\ (B\ O + D\ O)$$ for B C=D C because triangle A B D is an equilateral triangle (having its three sides perpendicular to the sides of the equilateral triangle R L F) and A C is the perpendicular bisector (being parallel to R L and therefore perpendicular to BD).

$$\delta = \tfrac{1}{2}\ (N\ O_2 + M\ O_3)$$ for B O=N O_2 and D O=M O_3 because parallel lines included between parallel lines are equal.

$$= \tfrac{1}{2}\left(e_2\frac{2}{\sqrt{3}} + e_3\frac{2}{\sqrt{3}}\right)$$ for angle N O_2A_2=30°=angle M O_3A_3 and the secant of 30° $= \frac{2}{\sqrt{3}}$

$$Y = \frac{e_2 + e_3}{\sqrt{3}}$$

accurately drawn, with its center at the center of a graduated circle, they have evaluated E and the angle α geometrically instead of algebraically. In practice, this method is considerably easier than the original method.

It will be evident to the student of mathematics that Einthoven and his followers have used what is known as the polar system of coordinates, designating as E and α what the mathematician ordinarily calls ρ and θ. In July, 1916, after perusing H. B. Williams' paper,[6] I was led to investigate the properties of Einthoven's triangle and its application to electrocardiography. In this investigation a system of rectangular coordinates was employed, and the results have been so interesting and suggestive that it seems advisable to publish this method of analysis as a preliminary to the publication of the results that we have obtained by its use.

The basic principle of the method can be demonstrated by means of Figure 1. Instead of finding values E and α which correspond to ρ and θ in the polar system of coordinates, we have found two values which correspond to what are known as X and Y in the rectangular system of coördinates. These two values locate the point A, and, since the point O is fixed at the center of the triangle,[7] give us the same information that was given by E and the angle α.

But, although our values for X and Y give us the same information that was given by E and α, they give it in a much more useful form. In the first place, it is easier to visualize points located by rectangular than by polar coördinates. It is simpler to think of a point with the value $X = 4$, $Y = 3$ than it is to think of the same point with the value $\rho = 5$, $\theta = 37°$, or $E = 5$, $\alpha = 37°$. Again, it is simpler to chart a point

6. Williams, H. B.: On the Cause of the Phase Difference Frequently Observed Between Homonymous Peaks of the Electrocardiogram, Am. J. Physiol. **35**:292 (Oct.) 1914

7. See footnote to Figure 1.

located by rectangular coördinates than the same point located by polar coördinates. Ordinary cross section paper can be used, and there is little possibility of error. Furthermore, the mathematics involved in locating a point are simpler with rectangular coördinates, viz:

rectangular coördinates[8]	polar coördinates[8]
$X = \epsilon_1$	$a = \tan^{-1} \frac{2\epsilon_2 - \epsilon_1}{\epsilon_1 \sqrt{3}}$
$Y = \frac{\epsilon_2 + \epsilon_3}{\sqrt{3}}$	$E = \frac{\epsilon_1}{\cos a}$

But the greatest advantage to be obtained by the use of rectangular coördinates is due to the fact that it is comparatively easy with this system to plot consecutively the successive values of X and Y through a complete cardiac cycle and to connect these consecutive points with a fairly smooth curve which we shall call the "monocardiogram," for reasons which will appear later.

In order to understand the significance of this "monocardiogram," we shall revert for a moment to Einthoven's original discussion of the equilateral triangle. Einthoven,[9] speaking of the Q R S wave of the electrocardiogram, says: "The curve must represent, under all circumstances and in every moment the algebraic sum of all the potential differences which at that moment are developed in the heart." We shall try to express the same thought by saying that the point X, Y (A in Figure 1), which we locate by our system of coördinates, represents the "center of negativity" of the heart at that instant; meaning by "center of negativity" a point somewhat analogous to "center of gravity" and "center of mass." If at any moment there are present in the heart several (negative) electrical charges which have value (intensity, voltage) and position (direction) then the center of negativity is that point which represents the algebraic sum of all the potential differences. The line, E, in Einthoven's drawings, which connects this point with the center of the equilateral triangle will, by its projections on the three sides of the triangle, give the values of the galvanometer deflections (ordinates) for the three leads at that particular instant. By finding the location of the center of negativity at consecutive instants, and connecting the points thus found by a continuous line, we obtain a curve which represents the successive algebraic sums of the potential differences that develop in the heart during the cardiac cycle. This curve we have called the monocardiogram to distinguish it from the ordinary electrocardiogram, which is really a "tricardiogram" or a threefold derivative of the monocardiogram.

8. See Figure 1.
9. Lancet **1**:856, 1912.

The monocardiogram is really a fusion of the three leads of the electrocardiogram into a single curve by an algebraic reversal of the process by which three leads are obtained from one heart. Its study brings us much nearer the real electrical events of the cardiac cycle than does the study of the ordinary E. K. G., or tricardiogram which is derived from it by our present method of leading off. Figure 2 illustrates this fact. It shows the monocardiogram of the Q R S deflection taken from an electrocardiogram published by Einthoven (Fig. 8)[1] and used by Einthoven as a demonstration in his original description of

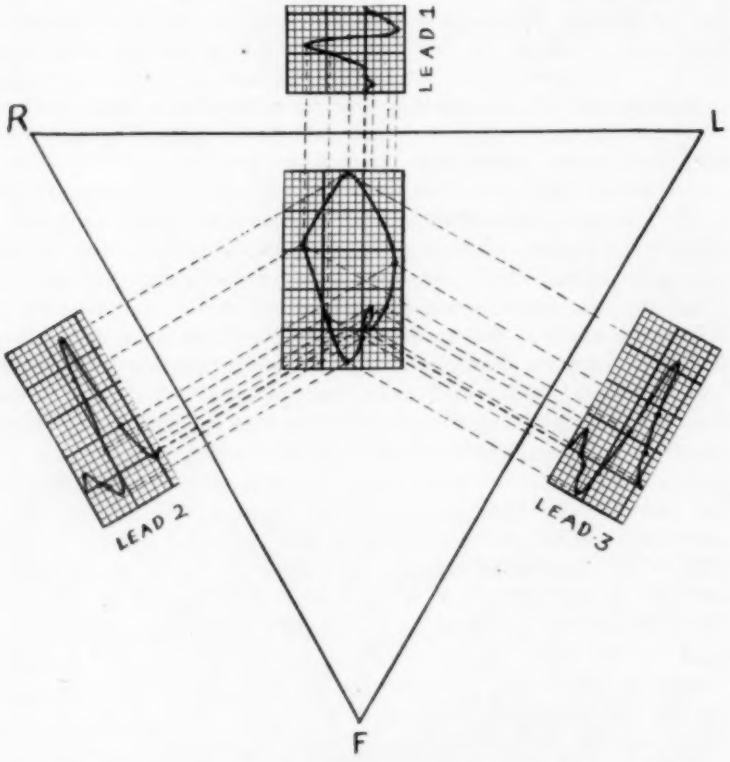

Fig 2.—This figure shows the monocardiogram which is derived from an electrocardiogram published by Einthoven (Fig. 8).[1] It can be seen that the three leads of the electrocardiogram are really derivatives of the monocardiogram, obtained by successive projections of the monocardiogram on the three sides of the equilateral triangle.

Note that in this monocardiogram, as in all the others shown in this article, the right side is on the observer's left. This is in accordance with ordinary cardiographic usage as regards Einthoven's triangle and facilitates interpretation.

the equilateral triangle. It can be seen that leads I, II and III are really derivatives obtained by successive projections of a vector connecting the center of our triangle with the successive positions of the center of negativity. Thus the monocardiogram represents, as nearly as can be represented in a plane figure, the actual electrical events of a cardiac cycle.

The direction and shape of the monocardiogram have an anatomic significance which is indicated only obscurely by the direction and shape of the ordinary electrocardiogram. The shape of the ordinary E. K. G. may be considered the result of the projection of the monocardiogram (M. C. G.) on the sides of an equilateral triangle, and thus the anatomic significance becomes distorted and obscured, but the M. C. G. itself owes its shape to the actual electrical events of the cardiac cycle and shows the successive relative positions of the center of negativity. Thus, it affords us a method of localizing, in a plane, various parts of the cardiac musculature; of analyzing an E. K. G. with regard to its anatomic significance; of determining what part of the cardiac musculature is responsible for various types of bizarre and abnormal E. K. G.'s, and of locating the site of origin of extrasystoles. By means of three leads taken in a horizontal plane and similarly analyzed we can obtain a "transverse monocardiogram" and get a three dimensional view of events during the cardiac cycle. It is our intention in further communications to discuss the points just mentioned and more especially to use the monocardiogram for the analysis of E. K. G.'s in which it is assumed that there are defects in various localized regions of the cardiac musculature: i. e., in cases of subendocardial myocarditis as described by Oppenheimer and Rothschild.[10]

For the application of our method to the analysis of an electrocardiogram it is not absolutely necessary to have simultaneous E. K. G.'s of the several leads. Provided the string has been carefully standardized it is quite practicable to proceed as follows:

1. By means of a camera lucida drawing, photographic enlargement, or by examination of the film with a microscope a series of careful measurements of a complete heart cycle is made for each lead. If there is evidence of respiratory or sinus arrhythmia care must be taken to select cycles which are in the same phase. The values of the ordinates are measured in millimeters for every hundredth of a second or less.

2. By the method of trial and error the three series of measurements are so arranged that for every moment during the cardiac cycle

10. Oppenheimer, B. S., and Rothschild, M. A.: Electrocardiographic Changes Associated with Myocardial Involvement, J. A. M. A. **69**:429 (Aug. 11) 1917.

lead II minus lead I equals lead III. In most curves, especially those with high peaks, this is a fairly easy matter.

3. The value for X for each moment (0.01 second) is known, for it is the value of lead I (Fig. 1), but the value of Y must be calculated as follows: divide the algebraic sum of leads II and III by the square root of 3. This is done by means of Table 1, and gives us the successive value of Y.

4. The successive positions of the point X, Y are plotted and connected with a fairly smooth curve, thus giving the monocardiogram.

Figure 3 illustrates the method of procedure. The camera lucida enlargement of the E. K. G. is shown; the values of the three leads for every hundredth of a second are shown properly arranged; the values of Y are shown calculated, and the monocardiogram resulting is shown.

Table 1.—This table is used for the calculation of the value Y $\left(\frac{e_2 + e_3}{\sqrt{3}}\right)$

It is used like a logarithm table. For example: at the instant labelled 20 in the table in Figure 3, the ordinate in lead II measured 9.7 mm., and the ordinate in lead III measured —.8 mm. The algebraic sum of 9.7 and —.8 is 8.9. If we look this number up in our table we use the horizontal row labelled 8 and the vertical row labelled 9. The number which we find at the intersection of these two rows is 5.138 and thus our value for Y is approximately 5.1. The values for Y at other instants were found in the same manner by adding the values of leads II and III and using the table to simplify the process of dividing by $\sqrt{3}$.

$\sqrt{3} = 1.7320+$

$\frac{e_2 + e_3}{\sqrt{3}}$	0	1	2	3	4	5	6	7	8	9	Differences
0		0.0577	0.1155	0.1732	0.2309	0.2887	0.3464	0.4041	0.4619	0.5196	
1	0.57735	0.6351	0.6928	0.7506	0.8083	0.8660	0.9238	0.9815	1.039	1.097	1. 0.00577
2	1.1547	1.212	1.270	1.328	1.386	1.443	1.501	1.559	1.617	1.674	2. 0.01155
3	1.7321	1.790	1.848	1.905	1.963	2.021	2.079	2.136	2.194	2.252	3. 0.01732
4	2.3094	2.367	2.425	2.483	2.540	2.598	2.656	2.714	2.771	2.829	4. 0.02309
5	2.8868	2.944	3.002	3.060	3.118	3.175	3.233	3.291	3.349	3.406	5. 0.02887
6	3.4641	3.522	3.580	3.637	3.695	3.753	3.811	3.868	3.926	3.984	6. 0.03464
7	4.0415	4.099	4.157	4.215	4.272	4.330	4.388	4.446	4.503	4.561	7. 0.04041
8	4.6188	4.677	4.734	4.792	4.850	4.907	4.965	5.023	5.081	5.138	8. 0.04619
9	5.1962	5.254	5.312	5.369	5.427	5.485	5.543	5.600	5.658	5.716	9. 0.05196

The use of simultaneous electrocardiograms is theoretically desirable, but we are not confined to such simultaneous records in the employment of this method. Successive heart cycles in an individual are so nearly alike that, provided proper precautions are exercised in the choice of cycles, the rule, lead II minus lead I equals lead III, holds for practical purposes. In practice we have found it possible to apply this method of analysis to the ordinary E. K. G. as usually taken.

Figure 4 shows a monocardiogram derived from one of the rare electrocardiograms in which all three leads were taken simultaneously. The original E. K. G. was published by Einthoven, Bergansius and

	X			Y
	Lead 1	Lead 2	Lead 3	$\frac{2+3}{\sqrt{3}}$
0	0	0	0	0
1	0.1	0.1	0	0.06
2	0.4	0.4	0	0.2
3	0.7	0.7	0	0.4
4	1.0	1.0	0	0.6
5	1.3	1.3	0	0.75
6	1.0	1.0	0	0.6
7	0.8	0.8	0	0.46
8	0.5	0.4	−0.1	0.17
9	0.1	−0.2	−0.3	−0.3
10	−0.3	−0.4	−0.1	−0.3
11	−0.5	−0.3	0	−0.17
12	−0.3	−0.3	0	−0.17
13	−0.3	−0.3	0	−0.17
14	−0.3	−0.3	0	−0.17
15	−0.3	−0.3	0	−0.17
16	−0.3	−0.3	0	−0.17
17	−0.3	−0.3	0	−0.17
18	−0.3	−0.3	0	−0.17
19	0	0.4	0.4	0.46
20	10.5	9.7	−0.8	8.1
21	8.2	12.0	3.8	9.3
22	5	8	3	6.4
23	0	2	2	2.8
24	−0.5	−0.2	0.3	0.06
25	−0.3	−0.3	0	−0.17
26	−0.3	−0.3	0	−0.17
27	−0.3	−0.3	0	−0.17
28	−0.2	−0.2	0	−0.1
29	−0.1	−0.1	0	−0.06
30	0	0	0	0
31	0.1	0.1	0	0.06
32	0.2	0.2	0	0.1
33	0.4	0.4	0	0.2
34	0.5	0.5	0	0.3
35	0.6	0.6	0	0.35
36	0.7	0.7	0	0.4
37	0.7	0.7	0	0.4
38	0.8	0.8	0	0.46
39	0.8	0.8	0	0.46
40	0.9	0.9	0	0.5
41	0.9	0.9	0	0.5
42	0.9	0.8	−0.1	0.4
43	0.9	0.6	−0.3	0.17
44	0.8	0.3	−0.5	−0.1
45	0.7	0.2	−0.5	−0.17
46	0.5	0.1	−0.4	−0.17
47	0.3	0	−0.3	−0.17
48	0.2	0	−0.2	−0.1
49	0.1	0	−0.1	−0.06
50	0	0	0	0

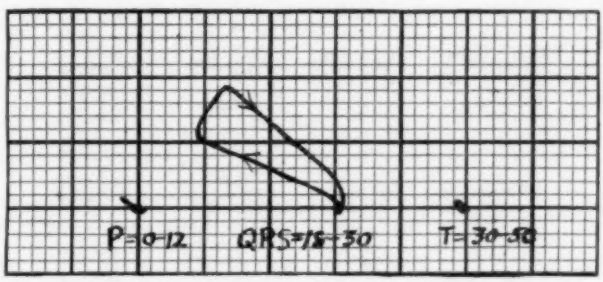

Fig. 3.—This figure shows the method of obtaining a monocardiogram. Above, to the left, is shown a camera lucida drawing of the three leads of an electrocardiogram. The ordinates represent 0.04 second and the abscissae represent 0.1 millivolt. To the right is shown a table of values of the ordinates of the three leads for every 0.01 second properly arranged so that lead II minus lead I equals lead III for every instant. The fourth column of figures in the table gives the values of Y calculated by means of Table 1. Below is shown the monocardiogram plotted by connecting successive values of the point, X, Y, with a smooth curve. The P, QRS, and T deflections are plotted separately. Positive values of X are plotted to the observer's left, for this is taken as the right side. Positive values of Y are plotted above the line, as is usual.

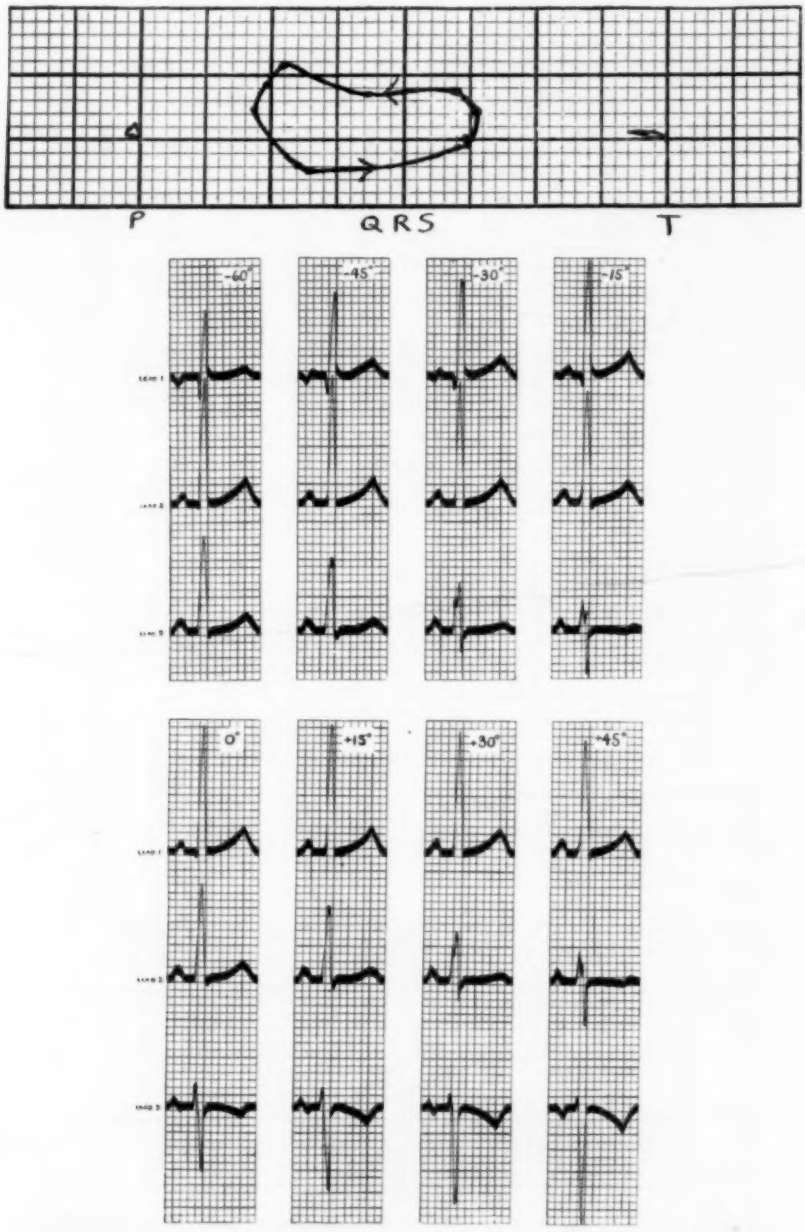

Fig. 4.—This shows the monocardiogram derived from an electrocardiogram published by Einthoven, Bergansius, and Bijtel[n] (Fig. 3, Cycle 2). From this E.K.G. (which is one of the very rare published electrocardiograms taken simultaneously in all three leads by means of three galvanometers) we have derived the monocardiogram, shown above. Below the monocardiogram are shown eight pairs of derived electrocardiograms. These were *derived* from the monocardiogram by a method similar to that illustrated in Figure 2 and they show the effect that rotation of the heart's axis would have on the electrocardiogram. We have followed customary trigometrical notation and called clockwise rotation negative and counterclockwise rotation positive. Thus by $+30°$ we mean that the heart is so rotated that the apex approaches the patient's left shoulder.

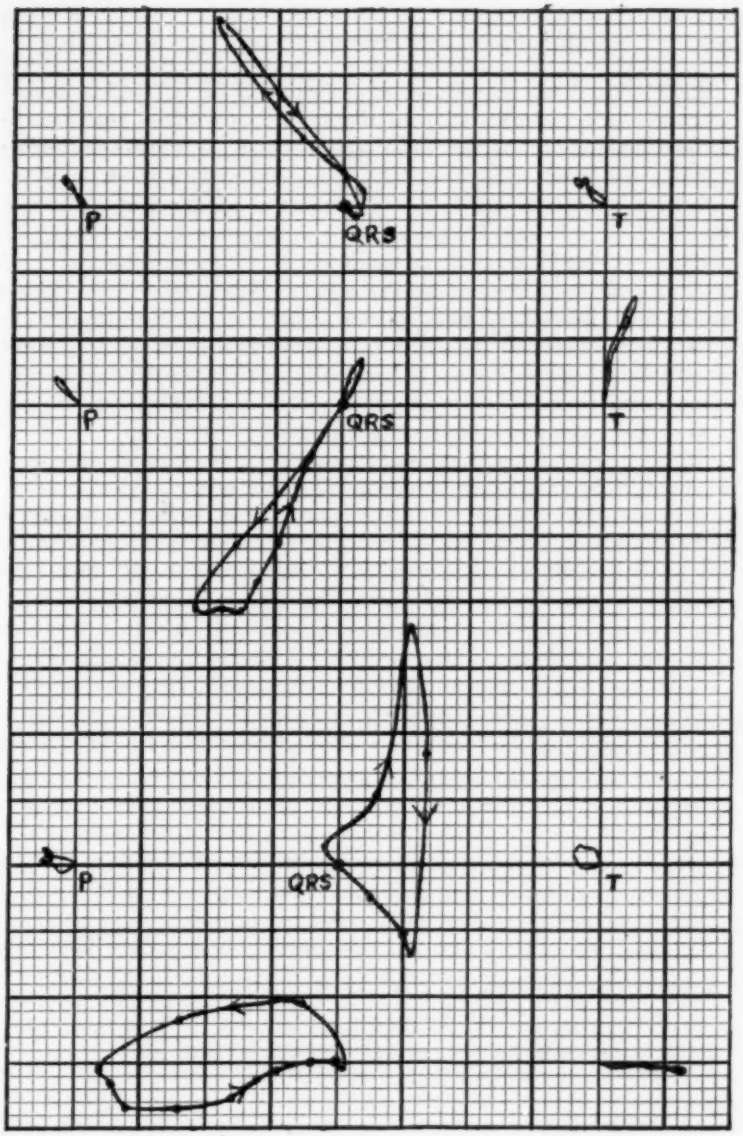

Fig. 5.—The uppermost monocardiogram is that of a normal heart. The second monocardiogram was derived from an E.K.G. which showed a characteristic *left* ventricular preponderance (main deflection upright in lead I and inverted in lead III).

The third monocardiogram was derived from an E.K.G. which showed a characteristic *right* ventricular preponderance.

The lowermost monocardiogram was derived from the electrocardiogram of a ventricular extrasystole. It points definitely to the right ventricle (observer's left).

Bijtel.[11] Our figure shows a series of derived E. K. G.'s which demonstrate the effect that rotation of the heart's axis would have on the ordinary electrocardiogram. The series of E. K. G.'s was obtained by rotating the monocardiogram and plotting the various resulting E. K. G.'s by a method similar to that illustrated in Figure 2. In Figure 2 the M. C. G. is derived from the E. K. G. By reversing our procedure, we can plot the E. K. G. from the M. C. G. By taking the M. C. G. and rotating it 15 degrees we can plot out the E. K. G. that would result if the heart itself were rotated 15 degrees. In this way we can obtain a series of E. K. G.'s that will show the effect of rotation of the heart's axis on the normal E. K. G. During normal respiration changes occur in the E. K. G. which are probably due to a combination of rotation of the heart's axis and nervous effects.[3]

Monocardiograms of a normal heart, of left ventricular preponderance, of right ventricular preponderance, and of a ventricular extrasystole are shown in Figure 5. It is interesting to note that in ventricular preponderance, the preponderant or thickened ventricle shows a tardiness in electrical response which causes a shifting of the center of negativity to the side opposite the preponderant ventricle and thus gives E. K. G.'s which are characteristic of preponderance. It can be seen that the different electrocardiograms which are characteristic of various types of cardiac abnormality give monocardiograms of every different form. The anatomical significance of the monocardiogram gives us reason to hope that this method of analysis will lead to closer correlation between cardiographic and pathologic findings.

SUMMARY

1. A new method is presented by which the ordinary three leads of the electrocardiogram are combined in a single curve, the monocardiogram.

2. Usefulness of this method of analyzing the electrocardiogram is explained.

The writer wishes to acknowledge indebtedness to Dr. B. S. Oppenheimer for his assistance in the final preparation of this paper.

50 East 96th Street, New York.

11. Einthoven, W., Bergansius, F. L., and Bijtel, J.: Die gleichzeitige Registrierung elektrischer Erscheinungen mittels zwei oder mehr Galvanometer und ihre Anwendung auf die Elektrokardiographie, Arch. f. d. ges Physiol. **164**: 167, 1916.

IRRITATION OF THE VAGUS AND HEMORRHAGIC EROSIONS OF THE STOMACH *

KNUD NICOLAYSEN, M.D.

The so-called vegetative or autonomous peripheral nervous system, which consists of the vagus and the sympathetic, has been subjected to systematic investigation only recently. While numerous contributions have been made to the knowledge of the functions of this system, we are yet far from a clear understanding of its structure and mode of action. The ideas of Eppinger and Hess[1] concerning vagotony and sympatheticotony are well known, but a few points may be discussed. We know that the vegetative nervous system consists of the vagus and the sympathetic, that they are antagonistic in most cases, holding each other normally in equilibrium, and that there are a number of substances which act as irritants or as paralyzers of these nerves. Thus pilocarpin irritates, atropin paralyzes the vagus, while epinephrin irritates the sympathetic, definite sympathetic paralyzers not being known. The antagonistic relation between the sympathetic and the vagus results, generally speaking, in that paralysis of the sympathetic produces the same symptoms as irritation of the vagus and vice versa. It also appears as if disturbed correlation between the endocrine organs may cause diminished or increased tonus in the vagus or sympathetic, or both. The vagus is the secretory and motor nerve of the stomach; hypersecretion, hyperchlorhydria and pyloric spasms are believed to result from irritation of the vagus and to be symptoms of vagotony. The similarity of these symptoms with those of ulcer of the stomach has led to the belief by some that ulcer also is associated with a vagotonic condition. Petrin and Thorling examined eighteen patients with ulcer of the stomach as to their reaction to pilocarpin and atropin, on the one hand, and epinephrin on the other, and came to the conclusion that a pronounced vagotony is often present in patients with ulcer, whereas a definite sympatheticotony was observed only rarely, five of the patients reacting to atropin-pilocarpin as well as to epinephrin.

During recent years, a number of experimental investigations have been made in regard to the influence of the vegetative nervous system on the stomach, especially with respect to hemorrhages and erosions.

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* From the Pathologic-Anatomic Institute of the Rikshospital, Christiania.

1. Eppinger, H., and Hess, Leo: Zur Pathologie des vegetativen Nervensystems, Ztschr. f. klin. Med. **67**:345, 1909; **68**:205, 231, 1909.

2. Petrin, K., and Thorling, I.: Untersuchungen über das Vorkommen von Vagotonus und Sympathikotonus, Ztschr. f. klin. Med. **73**:27, 1911.

Finzi[3] removed one or both suprarenals in rabbits and dogs, and subsequently observed edema and hemorrhages in the gastric mucosa, degeneration of the epithelial cells, and even real ulceration; the greater the amount of suprarenal removed the more extensive the changes. After total extirpation, the animals lived only a few hours, but in some instances, in which a remnant of the suprarenal was left, the animals lived from fifty to sixty days. The changes in the gastric mucosa developed rapidly, but healed slowly with only slight tendency to scar formation. If epinephrin was given after the extirpation, changes in the stomach did not take place. In five cases of gastric and duodenal ulcer in man, he found changes in the suprarenal after death — thickening of the capsule, fatty changes and hemorrhages.

Friedman[4] observed erosions in the duodenum in dogs after repeated injections of epinephrin. He found that extirpation of one or both suprarenals, of one suprarenal and a lobe of the thyroid, or of a thyroid lobe alone, in dogs and rabbits, was followed by hemorrhages and erosions in the stomach except when the operation involved the suprarenals and the thyroid at the same time. Consequently, he concludes that the lesions in the mucosa of the stomach in suprarenal insufficiency are dependent on the integrity of the thyroid.

Mann[5] experimented on dogs and cats, removing both suprarenals in one or two sittings, and keeping the animals etherized until they died, usually from two to eight hours after the operations, but no ulcers resulted; removal of one suprarenal was followed by death in from five to 235 days, but no ulcers were found, except in one case; removal of both suprarenals in one or two sittings resulted in ulcers in the stomach or duodenum in 90 per cent. Mann holds that the ulcers developed as the animals became moribund. He saw two types, one superficial and diffuse—erosions—and the other a sharply defined ulcer.

Friedman reports that he was able to produce erosions in the stomach in three of four rabbits by injection of thyroid substance. Believing that these erosions were caused by vagotony due to hormones in the thyroid, he tried to cause vagotony in rabbits by injecting pilocarpin, and in the thirteen animals experimented on erosions were found in all in the stomach at the same time as salivation, diarrhea and increased secretion of bronchial mucus and of tears resulted. In nine animals injected alternately with pilocarpin and epinephrin, eight developed erosions in the stomach and the duodenum. He concludes

3. Finzi, Otello: Ueber Veränderungen der Magenschleimhaut bei Tieren nach Nebennierenexstirpation, Virchows Arch. f. path. Anat. **214**:413, 1913.

4. Friedman, G. A.: Experimental Production of Lesions, Erosions and Acute Ulcers in Rabbits by Repeated Injections of Pilocarpin and Adrenalin, J. M. Res. **38**:449, 1918; **32**:

5. Mann, Frank C.: A Study of the Gastric Ulcer Following Removal of the Adrenals, J. Exper. M. **23**:203, 1916.

that epinephrin, together with pilocarpin, acts particularly on the duodenal mucosa, while pilocarpin alone acts on the gastric mucosa. He allowed the animals to live only a few hours after the last injections of pilocarpin, and it is noteworthy that the erosions appeared very promptly.

The results discussed in the foregoing are of interest not only with respect to the actions of the vegetative nervous system and its relation to the endocrine organs, but also because they throw a new light on the genesis of hemorrhagic erosion and perhaps also of gastric and duodenal ulcer.

That irritation ("stimulation of the vagus or paralysis of the sympathetic") may cause changes in the lining of the stomach in animals has been established. The nature of these changes and their fate, as well as the histologic processes initiated, are, however, less clearly understood. It is these questions which I have studied in rabbits injected subcutaneously with 5 per cent. pilocarpin hydrochlorate.

In all, twenty-five animals were used. The stomach was examined in all cases after formol fixation; the sections were stained with hematoxylin and eosin, van Gieson's method and Gram's method. Jenner's stain as recommended by Heyrovsky[6] was also used. The experiments are not described in order but in groups, and the same animals may be considered under more than one group.

Of ten animals which received from 10 to 35 cg. pilocarpin in two or more injections of 5 cg. each, and all of which died or were killed within twenty-four hours, nine showed changes in the lining of the stomach, three had in addition erosions or ulcers in the duodenum, only one animal being free from changes after twenty-four hours. This animal reacted to the injections with only slight salivation, whereas all the other animals immediately after the injection presented salivation, lacrimation, diarrhea and rapid respiration. Each animal, however, did not react in proportion to the amount of pilocarpin injected, and animals receiving the same amount of pilocarpin reacted in different degree; thus two died after they had received 10 cg., one two hours and the other twenty-four hours after the injection, and without any other apparent cause for death than increasing respiratory difficulties. The animals which died after two hours had extensive fat necrosis as demonstrated by Benda's reaction, as well as being evident macroscopically. In another animal, which had received 17.5 cg. of pilocarpin, and which died after eighty-four hours, there was found fat necrosis also. It is known that irritation of the vagus causes increased pancreatic secretion, but the reason that these two animals developed fat necrosis I have not tried to determine. The rabbit which received the greatest amount of pilocarpin, 35 cg., was moribund at the end of twenty-four hours and was killed; one rabbit is not included among the ten because it lived for seventy-two hours, during which time it received 2.5 cg. four times, dying without any other cause than pilocarpin intoxication. If we exclude the two rabbits which died with fat necrosis, we see that altogether three of twenty-five animals were killed directly by pilocarpin.

As there are persons with vagotony, it is reasonable to assume that there may be vagotonic animals also, and, as we shall see, there are certain signs

6. Heyrovsky, Hans: Histologische Untersuchungen der Magenschleimhaut bei Ulcus ventriculi und Carcinom, Deutsch. Ztschr. f. Chir. **122**:359, 1913.

which indicate that the animals which died were previously vagotonic. Eosinophilia is a well known sign of vagotony. Rabbits, however, have not only from 1 to 3 per cent. eosinophilic leukocytes normally, but most of the leukocytes in these animals are "pseudoeosinophils." In twenty-five rabbits I found 30 per cent. of the leukocytes to be acidophil, and that after injection of pilocarpin the number of acidophil cells increases rapidly in the course of a couple of hours, whereupon the number returns to normal. In fourteen animals, examination of the blood by Jenner's method after injection of pilocarpin, 200 leukocytes being counted each time, showed that ten of the animals on an average had 22 per cent. acidophils and 78 per cent. other leukocytes before the injection, and after the injection the percentages were 67 acidophils and 33 nonacidophils. Four animals were found to have a larger percentage than usual of acidophils before injection, and it is of great interest to note that these four animals all died, three of them as the direct result of pilocarpin

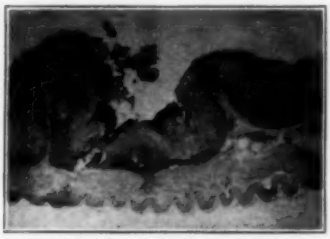

Fig. 1.—Hemorrhage into the mucosa in the bottom of a fold, the epithelium absent; × 20.

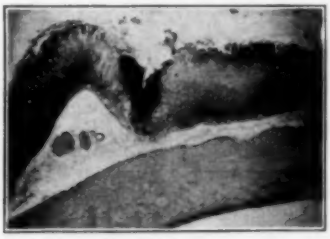

Fig. 2.—Definite loss of substance in five hours; × 20.

intoxication and the fourth from fat necrosis. Two of the animals which died from pilocarpin directly received only 10 cg.; these animals had 60 per cent. eosinophils before the injection, and there was hardly any increase in these cells afterward. It appears, then, when we consider the blood picture before and after injection of pilocarpin in the other rabbits in this series, that the acidophilia in the animals which died may be regarded as indicating an existing vagotony.

In order to learn how the erosions in the stomach developed, I examined this organ in twelve rabbits, all of which had received from 10 to 15 cg. of pilocarpin and which died or were killed between two hours and eighteen days after the injection. The erosions, which appeared as dark brown points or stripes, with more or less definite loss of substance, were found in all parts of the stomach, the number varying greatly even with the same dose of pilocarpin. The mucosa was covered with a good deal of mucus in the animals examined about twelve hours after the injection. The first change seemed to

be a hemorrhage into the mucosa (Fig. 1), either superficial or extending down to the muscularis mucosae, but always largest at the surface; these hemorrhages were most often round and then rarely more than about 2 mm. in diameter; at other times the hemorrhage was more linear, reaching a length of 1 cm. at the most. Corresponding to the extravasation there would form, little by little, losses of substance, which would be apparent as early as in two hours. The extravasated blood underwent the usual changes, with the formation of a brownish pigment. The lower part of the mucosa, which was not affected by the extravasation, had normal glands at the end of two hours. At the end of five hours the

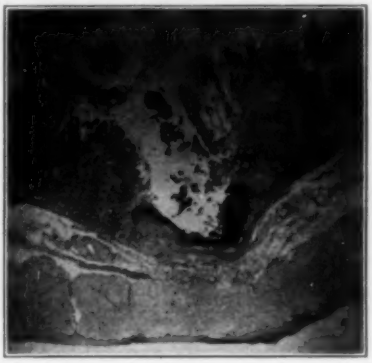

Fig. 3.—Loss of substance extending almost to the muscularis mucosae; × 20.

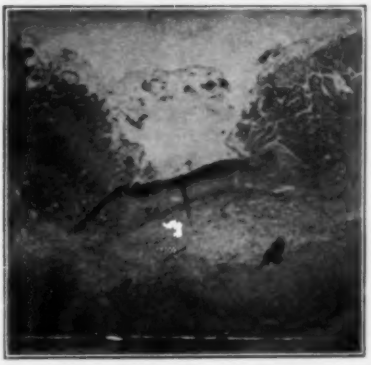

Fig. 4.—All blood pigment removed; × 20.

defect was larger, and round cell infiltration and edema made their appearance around it (Fig. 2). The defect now enlarged according to the extent of the primary hemorrhage. In the same stomach there would be found after twenty-four hours both wholly superficial defects, nearly free from pigment, as well as narrow slits about to close, and larger losses of substance reaching almost down to the muscularis mucosae, the bottom of which still was covered with pigment. About the defects would be exudate and fairly dense infiltration with cells down into the submucosa. In the bottom of the ulcer would be thrombotic vessels (Fig. 3). After forty-eight hours, the largest and deepest

erosion was observed, reaching almost down to the muscularis mucosae, all pigment being removed, the floor being formed by the deepest layer of the mucosa, the structure of which was no longer recognizable, inflammatory exudate and marked leukocytic infiltration extending through the submucosa, in which were thrombotic vessels. The mucosa, which was edematous and

Fig. 5.—The mucosa seems to have spread out from both sides over the floor which lies on the muscularis mucosae; × 45.

Fig. 6.—Showing newly formed glandular tubules at the bottom; × 45.

infiltrated with blood about the erosion, had folded itself definitely over the margins (Fig. 4) and the process appeared to have become arrested.

After seventy-two hours, the erosions clearly were about to heal. They appeared smaller; the hemorrhagic crust was nearly all removed. In the larger erosions the mucosa had spread itself over the bottom, in which were brownish

pigment and leukocytes (Fig. 5). The smaller erosions were covered over, and their site indicated by remnants of blood and pigment along the borders.

In two rabbits which were killed after six hours, erosions or scars could not be made out definitely, either macroscopically or microscopically; a third rabbit, however, presented a picture similar to that found after seventy-two hours. Of three rabbits which lived ten days, one showed no erosion; another had a small scar-like shrunken area in the larger curvature, shown microscopically to be a depression in the mucosa covered by epithelium without crypts, probably a scar after a deep erosion (Fig. 6); the third rabbit showed several erosions, all healing, the process apparently not having gone any further than in animals which had lived three to four days (Fig. 7); in one animal which lived eighteen days there were no erosions or scars.

The extravasation of blood into the mucosa, which forms the beginning of the erosion, is produced by an irritation of the vagus, but this does not explain how the hemorrhage takes place. That the cause is of

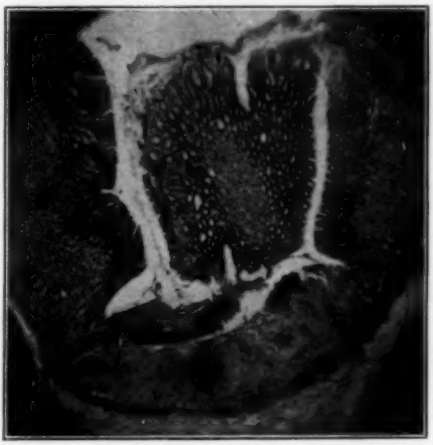

Fig. 7.—Mucosa about to cover the defect; × 45.

a vasomotor nature is not very likely the case, because the vessels of the stomach, so far as known, are innervated only by the sympathetic. It seems more likely that it concerns hemorrhages due to circulatory disturbances produced by contraction of the musculature of the stomach, especially the muscularis mucosae, through which the small vessels to the mucous membrane pass. The motor nerve of the stomach is the vagus as we know.

The loss of substance in the mucosa results from digestion of the tissue damaged by the hemorrhage, and the extent and depth of the loss depends on the extent of the hemorrhage. The quantity of pilocarpin injected seems to have no influence on the extent of the extravasation. It has been claimed that the injection of pilocarpin increases the secretion of the stomach, particularly the amount of free hydrochloric acid. In order to determine whether such

factors play any rôle in the development of the erosions, I aspirated gastric juice before and from two to three hours after the injection. The rabbits studied in this way were living on usual food, such as hay, cabbage and oats. The gastric juice was aspirated through a thin catheter, and usually from 2 to 6 c.c. was obtained each time. In twenty normal rabbits I found the relation between free hydrochloric acid and total acidity to be on the average 64:105. In eight rabbits the relation before injection of pilocarpin was 75:110, and from two to three hours after the injection it was 43:62. Later the relation was found to be variable. While the erosions develop as early as two hours after the injection of pilocarpin, the hydrochloric acid, as well as the total acidity, diminishes considerably during the first two or three hours after the injection. The stomach contents after the injection were rich in mucus; as stated, the mucosa was found covered with mucus at this time; it is, therefore, probable that it is the increased secretion of mucus which reduces the acidity. In any event, erosions undoubtedly develop even when the acid is reduced. Two animals were given sodium bicarbonate before and one and a half and four hours after the injection; the gastric contents then did not con-

Fig. 8.—Hemorrhage into the mucosa without destruction of the surface epithelium; × 45.

tain any hydrochloric acid, which was also the case when the animals were killed six hours after the injection. The usual hemorrhages were present in the mucosa but it was not possible to make out any loss of substance, and microscopically, the epithelium over the hemorrhagic area was well preserved everywhere (Fig. 8). Hence, it may be concluded that without hydrochloric acid there would be no erosions, that is to say, no loss of substance.

The erosions we have been studying are undoubtedly of the same kind as those which occur after extirpation of the suprarenals. The anatomic picture is precisely the same. Finzi and Mann believe that these erosions are the beginning of possible gastric ulcers. Finzi cites five cases of gastric and duodenal ulcer in which he found changes in the suprarenal after death. Friedman believes that some of the lesions which he observed would have healed in time, but that real ulcers might have developed on the basis of the lesions. My own observations, particularly as regards the appearance of the lesions, the fact that they never go deeper than the muscularis mucosae, and, finally, their marked tendency to heal, lead me to believe that they correspond to the hemorrhagic erosions seen in man. As these erosions in man cannot be regarded as a regular preliminary stage for the development of typical ulcer,

it would be unwarranted to conclude from the experimental and clinical observations at hand that ulcer of the stomach or duodenum results as a consequence of vagotony or vagus irritation.

HEMORRHAGIC EROSIONS

Hemorrhagic erosions occur in the human stomach and also in the duodenum. They are superficial, and, as the name indicates, they usually have a hemorrhagic floor. While it is true that there may be only a difference in degree between the simple erosion, especially if the hemorrhagic covering has been removed, and acute ulcer, there rarely are any difficulties in deciding after death whether erosion or ulcer is present. I do not deny that Mann and Friedman may have seen real ulcer develop on the basis of erosions, nor do I claim that an ulcer cannot develop from an erosion. All works on pathologic

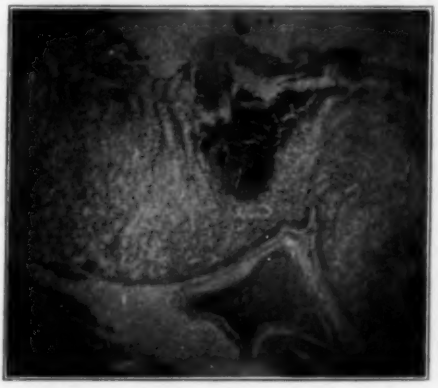

Fig. 9.—Erosion in the human stomach. Hemorrhage in the mucosa and beginning loss of substance; × 45.

anatomy treat hemorrhagic erosions as a peculiar process, which often is distinguished from postmortem changes only with difficulty; the ideas as to their mode of origin and their relation to ulcer are divided.

If the microscopic picture of a hemorrhagic erosion in the human stomach is compared with that of the lesions which develop in the stomach of the rabbit after injection of pilocarpin, there can be no doubt but that it concerns the same process (compare Fig. 2 and Fig. 9). The question consequently arises whether hemorrhagic erosions in man also depend on vagus irritation.

Beneke[7] has discussed this question in connection with observations of a large number of erosions studied after death, in which he no doubt has included certain other conditions than hemorrhagic erosion

7. Beneke, R.: Ueber die hämorrhagischen Erosionen des Magens (stigmata ventriculi), Verhandl. d. deutsch. path. Gesellsch. **12**:284, 1908.

strictly speaking. He regards the thrombosis in the neighborhood of the erosions as being secondary, and advances the idea that the erosions depend on a transitory ischemia in the mucous membrane produced by reflex irritation of certain nerves, because he found that in a high percentage of the cases there was disease of the central nervous system, and also because he found erosions in persons in whom the celiac ganglion might be injured by operation or peritonitis. While one would be inclined to agree with Beneke in regarding the thrombosis as secondary, his theory of a local, brief anemia is not convincing. To my mind, the primary lesion is a hemorrhage into the mucosa which reduces the vitality of the tissue. Whether this hemorrhage can be referred to a primary irritation of the vagus in the case of man as well as in the case of rabbits is a question on which I shall try to throw light by means of certain cases. I have gathered the cases of definite, unquestionable hemorrhagic erosions which I have observed in the course of the last two years in this institute. As definite hemorrhagic erosions I regard larger or smaller superficial defects in the mucosa with a dark brown floor, which have developed during life, as shown by thrombosis, pigmentation and more or less round cell infiltration. Hemorrhagic erosions of this sort have been observed in ten cases postmortem, five times in the stomach and in the duodenum. Fifteen erosions were examined microscopically; thrombi were not always present, bacteria were not demonstrable, and the mucous membrane around the erosions was always normal without signs of gastritis.

SUMMARY OF CASES

Case 1.—Man, aged 52; otitis media and diffuse meningitis; pulse, 120; died on day of admission to hospital.

Case 2.—Woman, aged 21; otitis media; operation; death five days later with large abscess in cerebellum. Pulse, at entrance, 88; day before death, 60; shortly before death, 120.

Case 3.—Man, aged 32; tuberculous meningitis; pulse 52; death.

Case 4.—Man, aged 37; diffuse meningitis after otitis media; pulse, 88; death.

Case 5.—Man, aged 25; miliary tuberculosis; marked meningeal symptoms; pulse from 88 to 100; death in four days.

Case 6.—Woman, aged 20; tuberculous meningitis; pulse increased gradually during ten days from 104 to 140.

Case 7.—Man, aged 25; in hospital two and a half months with tuberculosis of the lung and of the hilum glands, the pulse, at first very slow, became suddenly rapid; choked disks.

Case 8.—Man, aged 56; had sarcoma in lymph glands with metastases in the pleura; died from asphyxia; pulse at first 100, at time of death, fourteen days later, 144.

Case 9.—Man, aged 24; pulmonary disease following influenza; the upper and middle lobes infiltrated; thrombi in right ventricle.

Case 10.—Man, aged 60; intestinal obstruction; pulse, 60; diffuse peritonitis; operation; death soon after; pleural empyema.

COMMENT

There can hardly be any question that in the first group of six cases of this series irritation of the vagus was produced during the course of the illness which in every case was situated in the brain or its membranes. In the second group of three cases the disease involves the chest, the lungs and pleura being the seat of infiltrating processes. In Case 7 the very slow pulse, subsequently becoming rapid, indicates affection of the vagus. In a case of cancer of the breast with metastases in the lung and pleura described by Lyder Nicolaysen,[8] there was infiltration of the vagus and symptoms of vagus paralysis. In Case 10, one of peritonitis with empyema, it is possible that there may have been involvement of the nerves of the stomach in the abdomen as well as in the thorax, although the proof that such was the case cannot be supplied.

The vagus nerves and the nerves of the stomach in these ten cases should have been examined microscopically, but the material was gathered originally in the course of a study of ulcer of the stomach; it was only later that my attention was directed to the hemorrhagic erosions of the stomach in these cases. The result of the study shows that in most of the cases in which hemorrhagic erosions were found, there had been irritation of the vagus or the possibility of such irritation. To conclude from these cases that hemorrhagic erosions always result from irritation of the vagus does not seem warranted. It is possible that in some of these cases it concerns a coincidence. However, Benke's results and the pilocarpin experiments in rabbits favor the conclusion that vagus irritation may cause erosions. Further studies of suitable material should be made and with careful microscopic examination of the vagus.

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8. Nicolaysen, Lyder: Et Tilfälde av Vaguslammelse, Norsk Mag. f. Lägevidensk. **77**:948, 1916.

CLINICAL STUDIES ON THE RESPIRATION

VI. A COMPARISON OF VARIOUS STANDARDS FOR THE NORMAL VITAL CAPACITY OF THE LUNGS *

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As the clinical value of determinations of the vital capacity of the lungs becomes more clearly emphasized — in heart disease, in tuberculosis, in aeronautics, etc.—the problem of normal standards becomes increasingly important. For the clinician, the standard should require as few and simple measurements as are consistent with reasonable accuracy.

Since the earlier studies on this subject, it has been recognized that healthy individuals vary considerably in the volume of air which they can expire after a full inspiration. Age, sex, height, weight, the size and flexibility of the chest, muscular strength and physical training are factors which may singly or jointly affect the vital capacity. As an example, trained soldiers, and especially athletes, tend to show higher vital capacity readings than clerks of the same age, height and weight. The probability, therefore, of finding a single standard for all classes of individuals that does not involve numerous measurements and complicated formulas, and that is at the same time not subject to rather wide variations is, to say the least, remote.

Since Hutchinson's[1] admirable studies in 1846, various methods of approach to the problem have been tried. Hutchinson was the inventor of the spirometer, and his observations were unusually extensive and carefully made. After studying various measurements of the body in nearly two thousand healthy individuals from various classes and occupations, he concluded that the vital capacity varied more closely with differences in height than with any other known variable. Consequently, he adopted the following rule: "For every inch in height (from five feet to six feet), eight additional cubic inches of air at 60 F. are given out by a forced expiration."

Since this time the majority of workers have followed Hutchinson's method of using the height as the factor in determining the vital capacity normal for each individual. The method has been subject to much criticism on the basis that the individual variations for each height are too great, and numerous attempts have been made to substitute other measurements and formulas. Most of these have, however, been equally unsatisfactory, and have not been widely used.

Three of the more recent contributions must be considered in some detail. Peabody,[2] in his studies of the respiration, has demonstrated

* From the Medical Clinic of the Peter Bent Brigham Hospital and the Department of Medicine of the Harvard Medical School, Boston.

1. Hutchinson, Jonathan: Med. Chir. Tr., London **29**:137, 1846.

2. Peabody, F. W.: The Harvey Lectures, 1916-1917; also, Am. J. M. Sc. **155**:100, 1918.

the importance of reduction in the vital capacity as an index of the tendency to dyspnea in cardiac disease, and has emphasized the importance of vital capacity determinations in diagnosis, prognosis and treatment. He, with Wentworth, studying the vital capacities in a series of 140 healthy persons, largely medical students and nurses, found that, according to their height, they fell into three groups for each sex, and the average vital capacity for each group was taken as the normal standard. From ninety-six normal males, "Group I includes those who were 182.5 cm. (6 feet) tall or over, and the normal standard computed was 5,100 c.c. Group II consisted of men between 173.5 cm. (5 feet, 8½ inches) and 182.5 cm. (6 feet) tall, and the average vital capacity, which was 4,800 c.c., was taken for the normal. Group III was comprised of persons whose height was between 173.5 cm. (5 feet, 8½ inches) and 159.5 cm. (5 feet, 3 inches). The normal standard for this group was 4,000 c.c." Of these ninety-six men, 84 per cent. were within 10 per cent. of normal. "The women were also subdivided into three groups according to their height. Group I was composed of those who measured over 167 cm. (5 feet, 6 inches) tall, and the average vital capacity was 3,275 c.c. Group II consisted of those who were from 162 cm. (5 feet, 4 inches) up to and including 167 cm. (5 feet, 6 inches). The normal standard for this group was found to be 3,050 c.c. Group III was made up of persons from 154.5 cm. (5 feet, 1 inch) up to and including those who were 162 cm. (5 feet, 4 inches) tall. The standard vital capacity for this group was 2,825 c.c."

Peabody and Wentworth[3] also studied the relationship of the vital capacity to the body surface area in a small group of individuals, and finding a very close agreement, suggested that further studies on this line might be of considerable value.

Lundsgaard and Van Slyke[4] in a series of eighteen normal men and women found that the vital capacity varied more closely with the calculated chest volume than with the height. They determined the chest volume by making use of the following measurements. "The height of the chest is taken as the length of the sternum from incisio intraclavicularis to a point just below articulatio sternoxiphoidea. The depth is then taken as the horizontal distance from the middle of the sternum at the insertion of the third rib to the spinal column, and the breadth is the distance across the sixth ribs in the midaxillary line." The product of these figures taken with the chest at rest, the "middle chest volume," gives a value which is "approximately proportional" to the real chest volume. Certain precautions in taking these measurements must be observed, for the details of which the original article

3. Peabody, F. W., and Wentworth, J. A.: Arch. Int. Med. **20**:443 (Oct.) 1917.

4. Lundsgaard, Christen, and Van Slyke, Donald R.: J. Exper. M. **27**:65, 1918.

should be consulted. The average ratio, as found by Lundsgaard and Van Slyke, between the vital capacity and the middle chest volume was 45. $\left(\frac{100 \times \text{chest volume}}{\text{vital capacity}} = 45.\right)$ The observations by which this value was determined included both the males and the females.

Since the determinations of the present report were made, Dreyer[5] has published an excellent study of normal vital capacity standards. He shows that certain relations may be expressed, and arranges them in the order of their importance as follows:

"1. The vital capacity is a function of the *weight*. This can be expressed in the formula $\frac{W^n}{V.\ C.} = K$, where W is the net weight of the body expressed in grams, V. C., the vital capacity expressed in cubic centimeters, and the power n is approximately ⅔, though more accurately 0.72, and K is a constant. As it is already established that $\frac{W^n}{S} = K_2$ where W = net weight, S = body surface, and the power n is approximately ⅔ though more accurately 0.72, it follows that *the vital capacity is a simple function of the body surface*. In other words, that the smaller and lighter individual, with his relatively larger surface, has a greater vital capacity per unit of body weight than the larger individual.

2. The relation between the vital capacity and *stem length* can be correctly expressed by the formula $\frac{V.\ C.}{\lambda^n} = K_3$ where λ = stem length in centimeters, V. C. = vital capacity in cubic centimeters, the power n is approximately 2, and K_3 is a constant.

3. The relation between vital capacity and *circumference of chest* can be expressed by the formula $\frac{Ch.^n}{V.\ C.} = K_4$ where Ch. = circumference of chest expressed in centimeters, V. C. = vital capacity expressed in cubic centimeters, the power n is approximately 2, and K_4 is a constant.

4. Finally, $\frac{\lambda \times Ch.}{V.\ C.} = K_5$ where λ = stem length in centimeters, Ch. = circumference of chest in centimeters, V. C. = the vital capacity in cubic centimeters, and K_5 is a constant."

In applying these formulas, Dreyer found that the limit of error in the relation between the body surface and the vital capacity was comparatively slight, but becomes progressively greater in the succeeding formulas. He discards standards based on the height alone as being subject to too wide individual variations.

The formula $\frac{W^{\frac{2}{3}}}{S} = K$ is that of Meeh modified to $\frac{W^{0.72}}{S} = K$ in earlier studies of Dreyer with Ray and Walker[6] as being more nearly correct for determining the area of body surface.

5. Dreyer, Georges: Lancet **2**:227 (Aug. 9) 1919.
6. Dreyer, Ray and Walker: Proc. Roy. Soc. Med., Series B. **86**:39, 56, 1912.

It is suggested that the other formulas, though showing greater inaccuracies, may be of considerable value in determinations in pathologic cases where the weight has become abnormal.

The average value of the constant K in the formula, $\frac{W^n}{V.C.} = K$, determined in Dreyer's series of sixteen carefully studied persons was found to be 0.380 when the power n is taken as $\frac{2}{3}$ and 0.690 if 0.72 is taken as the value of n.

Professor Dreyer carefully points out, however, that there is a variation in the value of K if groups of individuals are studied whose nature of life and habits are distinctly different. This variation has previously been mentioned and suggests that in applying such standards for comparison of vital capacities, values must be determined for the various important classes of individuals and that these must be revised as conditions of life change in order to maintain a high degree of accuracy.

Lundsgaard and Van Slyke and Dreyer have shown the importance of vital capacity measurements in studying cases of pulmonary tuberculosis and their value in diagnosis, in prognosis and in gaging the effect of treatment.

The observations reported in this paper were undertaken for the purpose of applying various standards to the same group of individuals so that the variations in these standards might be compared.

The eighty-five men were nearly all members of the first year class in the Harvard Medical School, and were unselected, except that all were free from pulmonary or cardiac disease. They showed rather wide variation in physical type, from the habitually sedentary student to the college athlete. They, therefore, represent fairly well the average young men of their age seen in every-day life. The women were nearly all nurses from the Peter Bent Brigham Hospital, and were somewhat more carefully selected in that all were required to pass physical examinations before being admitted to the training school. No further selection than this was made.

The following measurements were recorded: Age, height in cm. without shoes, weight in kg. without clothes, chest volume by the method of Lundsgaard and Van Slyke, and the vital capacity in c.c. The latter was determined with the simple calibrated cylindrical spirometer of about eight liters capacity as described by Peabody. Several trials were allowed, a minimum of three, and the largest expiration recorded was taken as the vital capacity. From the height and weight the surface area was computed by the formula of DuBois and DuBois,[7] area (sq. cm.) $= \text{wt.}^{0.425} \times \text{ht.}^{0.725} \times 71.84$, the weight being in grams and the height in centimeters. The formula has been

7. DuBois, Delafield and DuBois, Eugene F.: Arch. Int. Med. **15**:868, Pt. 2 (June) 1915.

shown to be more accurate than Meeh's formula $\frac{W^{\frac{2}{3}}}{S} = K$. In order to eliminate extensive calculations, DuBois and DuBois have published a graphic chart by which the surface area can readily be determined if the height and weight are known. This method was used.

The data on the men and women were kept separate, and are tabulated in Tables 1 and 2. Values for the direct ratio between the vital capacity and height were computed and the average for the men was found to be 26.5. Since there is a comparatively large number of men with athletic training in the group who have unusually high vital capacities, the value 25 was arbitrarily chosen as being for practical purposes near to the normal of the average individual. And further, since all known pathologic conditions affecting the vital capacity do so by reducing it (witness heart disease and tuberculosis) it is much better to have standards which err in relation to high normals than to low normals. The data on the normals of Dr. Peabody were made available, and the average for the same ratio in his men was found to be 26.3. For the women the actual average was 20.6. The value 20 was assumed as the standard. Using 25:1 as the ratio for men and 20:1 as the ratio for women, 63 per cent. of the combined groups (129 persons) were seen to have vital capacities within 10 per cent. of the assumed normal. Only 5 per cent. of the group fell below 90 per cent. of the normal. The remaining 22 per cent. were higher than normal and were chiefly represented by those individuals having athletic training.

Using Peabody's group standards, 54 per cent. of the combined groups had vital capacities within 10 per cent. of the normal and 10 per cent. of the remainder were below 90 per cent. It is interesting that Peabody found such a close agreement in his series, using these standards. However, there are obvious objections to this method which those who have used the standard have undoubtedly discovered. The chief of these is the wide differences found in individuals whose height places them at the extremes of the various groups. For instance, a man 174 cm. tall, by this method should have a vital capacity of 4,800 c.c., while a man 173 cm. tall would be expected to have a vital capacity of only 4,000 c.c. In addition, the method is complicated and the various values are hard to remember.

The average value for the chest volume ratio was approximately 63 for the men and 56 for the women. With these values as standards, 69 per cent. of the combined groups were found to have vital capacities between 90 and 110 per cent., while 21.5 per cent. were below 90 per cent. On the other hand, when the value for the ratio adopted by Lundsgaard and Van Slyke (45) was used as the standard, only 8 per cent. of the 129 persons had vital capacities within 10 per cent. of the normal and 81 per cent. were over 120 per cent. of the normal.

Finally, we find that the most consistent relationship exists between the vital capacity and the area of the body surface. The actual average for the men was 2.61 L. per sq. m. of body surface, and for the women 2.07 L. per sq. m.; 2.5 L. per sq. m. and 2.0 L. per sq. m. were chosen as more convenient standards and as in the height ratio giving slightly less influence to the presence of the unusually high vital capacity found in some of the individuals observed. By these standards 71 per cent. were found to have vital capacities within 10 per cent. of the normal and only 5.5 per cent. were below 90 per cent. It was interesting and gratifying to discover that when the formula of Dreyer, $\frac{W^{0.72}}{V.C.} = K$) was used later, and the values for K were taken as the averages found in these two groups (in eighty-five men $K = 0.632$; in forty-four women $K = 0.807$), almost identical results were obtained, the number having vital capacities within 10 per cent. of the normal by this method being only about 2 per cent. less than when the formula of DuBois and DuBois was used.

In the accompanying chart curves have been constructed showing these results in graphic form. The ordinates represent the number of observations as expressed in per cent. of the combined groups, men and women, the abscissae represent the relation in per cent. to the various standards, the normal given as 100 per cent.

In Table 1 the asterisk before the initials indicates those men who have done more than the usual amount of athletic work. This consisted chiefly in high school and college foot ball, basket ball, track, base ball, swimming, rowing, etc. It is to be noted that all of the men having vital capacities of more than 5,300 c.c. are of this group. Six men having vital capacities of more than 5,000 c.c. but not more than 5,300 c.c. gave no history of unusual athletic training. For this trained group the average values for the various ratios may be seen in Table 3. They are noticeably higher than the averages for the whole group.

No particular reason was found for the few vital capacities that were considerably lower than the general average.

From these data, as well as from the work of Dreyer, it would appear that the most accurate method for calculating the normal vital capacity for an individual is from a standard based on the surface area. In using a value for this standard, whether as expressed in c.c. per square meter of body surface or an arithmetical value as a constant as in the formula $\frac{W^{0.72}}{V.C.} = K$, it would seem that allowance must be made for the past physical training and experience of the individual. Professor Dreyer's tabulation of the observations of Hutchinson on

TABLE 1.—Analysis of Findings in Eighty-Five Normal Men

	Age	Vital Capacity, C.c. (A)	Height, Cm. (B)	Weight, Kg. (C)	Body Surface Area, Sq. M. (D)	Chest Volume, 1 (E)	$\frac{A}{B}$	$\frac{A}{D}$	$\frac{100\ A}{E}$ (expressed in C.c.)	Percentage Relation to Standards				
										Peabody's Standards	$\frac{A}{B} = 25$	$\frac{A}{D} = 2.5$	$\frac{100\ A}{E} = 45$ (Lundsgaard and Van Slyke)	$\frac{100\ A}{E} = 62$ (Average of this group)
F. C. F.*	20	6,700	187.0	80.4	2.06	9.06	35.8	3.25	74.0	122	143	130	164	117
G. C. C.*	25	6,500	195.5	85.6	2.18	8.12	33.3	2.98	80.0	128	133	119	178	127
D. B.*	21	6,200	180.5	79.0	1.99	9.18	34.4	3.11	67.5	129	138	124	150	107
E. B. D.*	23	5,800	179.5	71.6	1.90	7.80	32.3	3.05	74.4	121	129	122	165	119
H. B. G.*	20	5,760	185.0	77.0	2.03	8.38	30.6	2.84	68.8	113	122	114	153	109
J. S.*	24	5,700	174.5	72.4	1.87	10.30	32.7	3.05	55.4	119	131	122	123	88
F. M. S.*	23	5,700	186.0	70.2	1.93	10.92	30.7	2.95	52.2	112	123	118	116	83
G. E. D.*	23	5,500	179.0	64.6	1.82	6.52	29.0	3.02	84.2	115	116	121	187	134
A. C. R.*	28	5,450	177.7	70.6	1.88	9.24	30.7	2.90	59.0	114	123	116	131	94
A. V. D.*	36	5,300	181.0	80.8	2.01	9.49	29.2	2.64	59.9	110	117	106	124	95
H. L. R.	22	5,300	168.0	63.3	1.72	7.66	31.5	3.08	69.2	133	126	123	154	110
F. F. M.*	33	5,300	181.5	70.4	1.90	8.82	29.2	2.79	60.1	110	117	112	134	96
R. C. McL.	22	5,300	181.8	74.4	1.95	6.54	29.2	2.72	81.0	110	117	109	162	129
M. R.	21	5,200	180.0	67.2	1.86	8.12	28.9	2.80	64.1	108	116	112	143	102
C. H. E.	30	5,200	175.5	61.5	1.76	6.87	29.6	2.95	75.7	108	118	118	168	120
W. W. H.*	23	5,200	173.5	65.0	1.78	7.06	30.0	2.92	73.4	108	120	117	163	112
K. L. M.*	21	5,200	174.5	64.4	1.78	7.70	29.8	2.92	67.5	108	119	117	150	107
R. L. L.	21	5,150	170.5	64.4	1.75	8.09	30.2	2.94	63.7	129	121	118	142	101
A. Q.	23	5,100	174.0	61.6	1.75	8.82	29.3	2.91	57.8	106	117	116	129	92
T. P. K.*	22	5,000	179.5	65.2	1.83	7.32	27.9	2.73	68.4	104	112	109	152	109
E. A. E.	30	5,000	175.0	78.5	1.94	9.64	28.5	2.58	51.9	104	114	103	115	82
R. A. D.	25	5,000	173.0	64.3	1.78	8.03	28.9	2.81	62.3	125	116	112	138	99
J. W. M.*	24	5,000	183.0	75.2	1.97	7.70	27.3	2.54	65.0	98	109	102	144	103
W. H. v. W.*	23	5,000	170.8	64.1	1.75	6.81	29.3	2.86	73.4	125	117	114	163	116
S. H.	24	4,900	166.8	65.0	1.73	7.84	29.7	2.87	63.3	124	119	115	141	100
D. C. G.	22	4,900	169.0	66.0	1.77	6.80	29.0	2.77	72.1	123	116	111	160	114
J. P.	36	4,900	169.0	72.0	1.83	9.45	29.0	2.68	51.8	122	116	107	115	82
H. J. S.*	24	4,900	172.5	68.2	1.81	6.94	28.4	2.71	70.6	123	114	108	157	112
S. G.	24	4,850	179.0	63.6	1.80	7.08	27.1	2.69	68.6	101	108	108	152	109
J. R. W.*	24	4,850	175.8	67.8	1.83	8.25	27.6	2.65	58.8	101	110	106	131	93
H. B.	24	4,850	175.0	60.5	1.74	8.10	27.7	2.79	59.9	101	111	112	133	95
G. W. T.*	22	4,800	171.0	65.0	1.77	8.02	28.1	2.71	59.9	120	112	108	133	95
T. L. P.	21	4,800	178.0	65.2	1.82	6.70	27.0	2.64	71.7	100	108	106	159	114
H. D.*	22	4,750	176.0	66.0	1.81	7.13	27.0	2.62	66.6	99	108	105	148	106
S. N. G	23	4,700	176.0	60.2	1.74	7.03	26.7	2.70	66.9	98	107	108	149	106
E. V. H	22	4,700	177.0	74.2	1.91	7.72	26.6	2.46	60.9	98	106	98	135	97

F. P. K	21	4,700	178.0	62.4	1.78	7.22	26.4	2.64	65.1	98	106	106	145	101
G. K.	21	4,700	171.0	63.5	1.75	7.18	27.5	2.69	65.5	118	110	108	147	104
M. J. M.*	21	4,700	182.0	70.5	1.91	7.40	25.8	2.46	63.6	98	103	96	141	101
L. W.	21	4,700	169.0	74.4	1.85	6.85	27.8	2.54	68.6	118	111	102	153	109
E. J. R.	22	4,650	170.4	63.6	1.74	8.10	27.3	2.69	57.5	116	109	108	128	91
L. W.	21	4,600	174.0	68.0	1.82	7.71	26.4	2.58	59.7	96	106	101	133	95
H. P. S.	21	4,600	173.5	65.2	1.79	6.25	26.5	2.57	73.6	96	106	103	164	117
F. V. G.*	22	4,600	173.5	68.9	1.84	7.79	26.5	2.50	59.0	96	106	100	131	94
J. L. G.	22	4,520	174.0	57.0	1.69	7.00	26.0	2.67	64.6	92	104	107	144	102
G. G. S.	19	4,500	167.3	62.5	1.70	6.73	26.9	2.65	66.8	113	108	106	149	106
H. B. S.	23	4,500	167.5	57.6	1.79	6.40	24.0	2.51	70.4	88	96	100	156	112
J. R. G.	25	4,500	170.0	53.5	1.62	6.03	26.5	2.78	74.6	113	106	111	166	118
R. W. B.	24	4,500	164.3	62.2	1.68	7.89	27.4	2.68	57.1	113	110	107	127	91
J. W. M.*	25	4,450	173.8	57.6	1.69	6.34	25.6	2.63	70.2	93	102	105	156	111
M.	22	4,400	161.5	59.5	1.63	7.40	27.3	2.70	59.5	110	109	108	132	95
W. A. K.	19	4,400	173.5	64.8	1.78	7.64	25.4	2.47	57.6	92	102	99	128	92
F. M. F.*	21	4,400	177.8	71.6	1.89	8.16	24.7	2.33	54.0	92	99	98	123	86
H. T. C.	18	4,400	183.0	70.8	1.92	9.81	24.1	2.29	44.9	86	97	92	100	71
W. P.	22	4,350	163.3	60.0	1.65	7.49	26.6	2.64	58.0	109	106	106	129	92
B. N. S.	21	4,300	169.0	67.4	1.78	6.86	25.5	2.42	62.7	108	102	97	140	100
R. L. M.	23	4,300	174.0	57.2	1.69	7.00	24.7	2.54	61.4	90	99	102	136	98
McK.	21	4,300	179.0	60.2	1.77	7.08	24.0	2.43	60.8	90	96	97	135	97
W. W. F.	26	4,300	167.5	58.8	1.67	8.26	25.7	2.57	52.0	108	103	103	116	83
D. H. F.	19	4,300	166.0	64.8	1.72	7.70	25.9	2.50	55.8	108	104	100	124	89
J. P. C.	21	4,250	172.5	62.2	1.74	6.24	24.6	2.44	68.1	106	98	98	151	108
E. C. S.	23	4,210	180.2	55.5	1.71	6.80	23.3	2.46	61.9	88	93	98	138	98
J. T. S.	21	4,200	175.6	65.8	1.81	8.10	23.9	2.32	52.0	88	96	93	116	83
C. W. S.	22	4,200	167.5	51.4	1.57	5.16	25.1	2.68	81.4	105	100	107	181	129
J. P. P.	26	4,200	172.0	57.3	1.68	6.47	24.4	2.50	64.8	105	98	100	144	103
C. F. O'B.*	23	4,200	165.0	56.3	1.62	5.38	25.5	2.59	78.1	105	102	104	174	124
B. I. G.	22	4,200	171.0	57.4	1.67	7.36	24.6	2.52	57.1	105	98	101	127	91
A. J. P.	23	4,100	171.5	57.0	1.67	8.92	23.9	2.45	46.0	108	96	98	102	73
T. J. C.	22	4,100	174.0	64.0	1.78	7.25	23.6	2.30	56.6	85	94	92	126	90
S. I. S.	22	4,050	166.3	59.8	1.67	7.62	24.4	2.43	53.1	101	98	97	118	84
P. J. K.	21	4,050	172.0	57.3	1.68	6.56	23.5	2.41	61.7	101	94	96	137	98
H. T. H.	23	4,050	172.2	60.9	1.72	7.00	23.5	2.35	57.9	101	94	94	129	92
H. I. B.	21	4,050	172.5	55.9	1.67	7.01	23.5	2.43	57.8	101	94	97	128	92
H. M.	20	4,000	169.5	60.0	1.69	6.60	23.6	2.37	60.6	100	94	95	135	96
M-L.	21	4,000	173.6	58.7	1.70	7.38	23.0	2.35	54.2	83	92	94	130	93
L. S.	21	3,950	169.0	58.8	1.68	5.76	23.4	2.35	68.6	99	94	94	152	109
C. A. B.	26	3,910	174.5	72.0	1.87	7.21	22.4	2.09	54.2	82	90	84	121	86
M. K.	21	3,900	160.6	53.4	1.55	5.65	24.3	2.52	69.0	98	97	101	153	109
B. E. B.	21	3,900	167.0	62.5	1.70	6.78	23.4	2.29	57.5	98	94	92	128	91
W. F. H.	22	3,750	175.5	58.8	1.72	5.82	21.4	2.18	64.4	78	86	87	143	102
J. G.	21	3,750	168.5	56.5	1.64	6.80	22.3	2.29	55.2	94	89	92	123	88
R. L. M.	22	3,650	160.7	57.3	1.60	5.72	22.7	2.28	63.9	91	91	91	142	101
M. F. C.	27	3,600	157.5	62.0	1.63	6.28	22.9	2.21	57.4	90	92	88	128	91
W. J. M.	22	3,500	162.8	56.0	1.60	6.53	21.5	2.19	53.6	88	86	88	119	85
E. A. McV.	23	3,400	166.9	58.0	1.65	6.79	20.4	2.06	50.1	85	82	82	111	80

* Men who have done more than the usual amount of athletic work.

TABLE 2.—Analysis of Findings in Forty-Four Normal Women

	Age	Vital Capacity, C.c. (A)	Height, Cm. (B)	Weight, Kg. (C)	Body Surface Area, Sq. M. (D)	Chest Volume, l (E)	$\frac{A}{B}$	$\frac{A}{D}$	$\frac{100\ A}{E}$ (expressed in C.c.)	Percentage Relation to Standards				
										Peabody's Standards	$\frac{A}{B} = 20$	$\frac{A}{D} = 2.0$	$\frac{100\ A}{E} = 45$ (Lundsgaard and Van Slyke)	$\frac{100\ A}{E} = 56$ (Average of this group)
I. G.	22	4,150	170.5	85.8	1.98	8.60	24.3	2.10	48.3	127	122	105	107	86
J. D.	19	4,000	168.9	61.2	1.67	6.57	24.4	2.40	61.0	131	122	120	135	109
A. F.	22	3,950	169.0	72.3	1.83	6.72	23.4	2.16	58.8	121	117	108	131	105
M. P.	22	3,900	160.4	51.6	1.58	6.06	24.3	2.55	64.0	128	122	128	142	114
L. V.	23	3,900	167.7	58.4	1.68	6.53	23.3	2.32	59.7	119	117	116	123	106
N. F.	22	3,900	171.6	54.6	1.64	5.94	22.7	2.38	65.7	119	114	119	146	117
M. G.	26	3,900	166.3	66.2	1.74	7.96	23.5	2.24	49.0	128	118	112	109	88
M. E.	28	3,800	164.9	69.6	1.77	7.90	23.0	2.15	48.2	125	115	108	107	86
E. J.	21	3,700	167.3	61.0	1.69	5.52	22.1	2.19	67.0	113	111	110	149	120
F. T.	29	3,700	166.6	60.2	1.68	6.20	22.2	2.20	59.7	121	111	110	133	107
H. L.	27	3,600	167.2	66.4	1.75	6.40	21.5	2.06	56.3	110	108	103	125	100
F. G.	24	3,600	163.5	61.2	1.67	6.60	22.0	2.15	54.6	115	110	108	121	98
M. R. S.	24	3,600	164.1	61.2	1.67	5.88	21.9	2.15	61.2	118	110	108	136	109
B. B.	30	3,550	167.2	62.0	1.70	6.84	21.2	2.09	52.0	108	106	105	115	93
G. P.	27	3,550	163.4	53.4	1.57	6.34	21.7	2.26	56.0	116	109	113	124	100
A. P.	21	3,500	170.8	60.4	1.70	5.64	20.5	2.06	62.0	107	103	102	138	111
H. B.	20	3,500	156.9	44.6	1.41	5.40	22.3	2.48	64.8	124	112	124	144	116
E. O.	26	3,500	168.3	64.8	1.74	6.72	20.8	2.01	52.1	107	104	101	116	93
M. M.	25	3,450	166.7	67.2	1.75	6.90	20.7	1.97	50.0	113	104	99	111	89
B. J.	20	3,350	156.8	62.0	1.62	7.31	21.4	2.07	45.8	118	107	104	102	82
J. H.	19	3,300	159.3	56.4	1.58	5.56	20.7	2.11	59.4	117	104	106	132	106
O. M.	25	3,300	159.7	50.0	1.50	5.10	20.7	2.20	64.6	117	104	110	144	115
B. G.	21	3,300	166.5	62.0	1.70	5.74	19.8	1.94	57.5	108	99	97	128	103
L. P.	21	3,300	160.5	49.2	1.50	5.34	20.6	2.20	61.8	117	103	110	137	110
P. K.	25	3,330	154.7	57.4	1.55	5.50	21.5	2.15	60.6	118	108	108	135	108
H. G.	23	3,250	164.0	52.6	1.57	5.70	19.8	2.07	57.0	107	99	104	127	102
M. K.	27	3,250	166.2	56.0	1.62	5.50	19.6	2.01	59.0	107	98	101	131	105
L. S.	27	3,200	162.4	59.4	1.64	4.92	19.7	1.95	65.0	105	99	98	145	116
B. H.	23	3,200	161.4	60.4	1.64	5.62	19.8	1.95	57.0	112	99	98	127	102
V. M.	20	3,200	168.0	50.7	1.53	5.52	19.6	2.09	58.0	105	98	105	129	104
A. M. H.	39	3,200	163.5	60.0	1.65	6.86	19.6	1.94	46.7	105	98	97	104	84
M. B.	22	3,150	161.5	50.6	1.52	6.15	19.5	2.07	51.4	112	98	104	114	92
M. G.	28	3,100	168.6	54.0	1.60	6.40	18.4	1.94	48.5	95	92	97	108	87
M. W.	24	3,100	160.7	64.2	1.68	6.73	19.3	1.84	46.1	110	97	92	102	82
H. N.	33	3,100	155.8	55.6	1.54	5.74	19.9	2.01	54.0	110	100	101	120	97
M. McD.	20	3,100	165.5	61.0	1.68	6.00	18.7	1.85	51.6	102	94	93	115	92
D. H.	19	3,000	159.5	52.2	1.52	5.52	18.8	1.97	54.4	106	94	99	121	97
R. C.	20	3,000	162.8	62.2	1.67	8.44	18.4	1.80	35.6	99	92	90	79	64
L. H.	18	3,000	165.7	61.6	1.68	5.00	18.1	1.79	60.0	99	91	90	133	107
M. D.	21	2,900	160.0	51.0	1.52	4.41	18.1	1.91	65.8	103	91	96	146	117
L. L.	26	2,800	155.7	58.6	1.59	5.74	18.0	1.76	48.7	99	90	88	108	87
R. M.	19	2,800	168.3	57.0	1.64	7.85	16.6	1.71	35.7	85	84	86	80	64
F. W.	24	2,600	163.7	42.1	1.42	3.82	15.9	1.83	68.0	85	80	92	151	121
E. C.	30	2,500	156.5	42.8	1.39	4.21	16.0	1.80	59.4	89	80	90	132	106

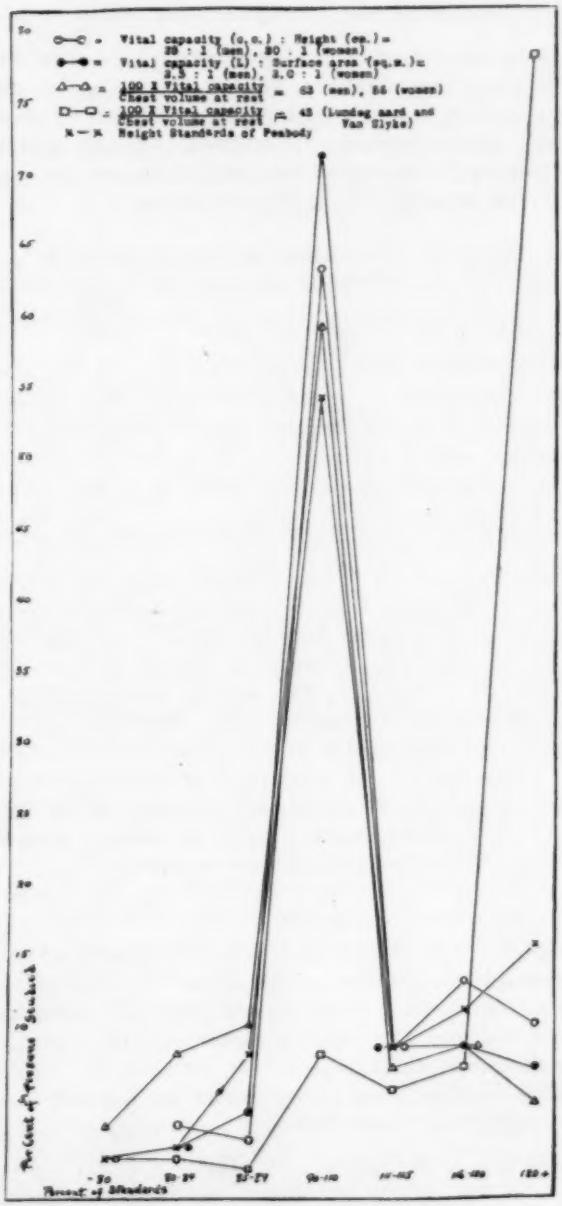
Vital capacity (c.c.) : Height (cm.) =
20 : 1 (men), 20 . 1 (women)
Vital capacity (L) : Surface area (sq.m.) =
2.3 : 1 (men), 2.0 : 1 (women)
100 X Vital capacity / Chest volume at rest = 53 (men), 56 (women)
100 X Vital capacity / Chest volume at rest = 45 (Lundeg aard and Van Slyke)
Height Standards of Peabody
Per Cent of Persons Studied
Percent of Standards
- 70
70-89
90-110
111-129
130+

Chart showing percentage of persons in relation to normal standards. Ordinates: Percentage of group (129 persons). Abscissae: Percentage of standards used. The group falling on the abscissa 90-110 includes those individuals whose vital capacities fell within 10 per cent .of the normal.

this basis is the most complete comparison of this type so far available. It is to be hoped that similar extensive observations of the more important groups representative of the habits of life of the present day may soon become available. In addition, it is very desirable that more observations be made on elderly individuals, for age apparently reduces the vital capacity to an appreciable extent.

TABLE 3.—SUMMARY OF RATIO VALUES

	Men	Women	Athletes
Vital capacity: height	25.0	20.0	29.0
Vital capacity: body surface area	2.5	2.0	2.8
100 × vital capacity: chest volume	62.0	56.0	67.0
$\frac{W^{0.075}}{V.\ C.}$	0.632	0.807	0.591
$\frac{W^{2/3}}{V.\ C.}$	0.350	0.450	0.326

For quick clinical work, where it is not practicable to obtain the net weight of the patient nor to make extensive measurements, a simple comparison between the vital capacity and the height will give a value which will closely approximate the normal for that individual, though individual variations by that method are greater than when the surface area is used. According to the chart, however, it is seen that practically the same number of low values were found by the two methods. While the greatest proportion of vital capacities studied were within 10 per cent. of the normal, too much weight should not be given to single determinations, unless a variation of more than 15 per cent. from the chosen standard is obtained.

SUMMARY

A group of 129 persons are studied for the purpose of comparing various standards for determining the normal vital capacity.

A standard based on the body surface area is advised, since it has been shown that the vital capacity varies with this function more uniformly than with others tried.

When the weight of the patient cannot be obtained, a standard based on the height is recommended.

I desire to express my appreciation to Miss B. I. Barker and Dr. T. D. Cunningham for their valuable assistance in accumulating and compiling the data used in these observations.

EXPERIMENTAL DETERMINATION OF THE INFLUENCE OF ABNORMAL CARDIAC RHYTHMS ON THE MECHANICAL EFFICIENCY OF THE HEART *

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INTRODUCTION

The occurrence of an abnormal cardiac rhythm clinically involves two important and essentially different considerations. First, the information it may give as to the general pathologic condition of the heart and the prognosis of the disease, and second, the mechanical influence it exerts on the pumping action of the heart. The normal heart beat, in which there is a regular succession of auricular systoles within certain rates, each of which is followed after a definite interval by contraction of the two ventricles, is best adapted to the function of the heart as a pump. Anything which seriously interferes with the normal rate or coordination of beats, interferes, to a certain extent, with the mechanical efficiency of the heart. An excessive rate of contraction, even though the regularity and coordination of beats is maintained, reduces the amount of blood pumped by the heart by shortening and rendering insufficient the period during which the ventricles fill with blood from the auricles.[1]

It is interesting to note in this connection that owing to the rapid period of ventricular filling immediately following ventricular systole, considerable increase in heart rate may occur without serious reduction of the amount of blood entering the ventricles during diastole. There is thus made possible a considerable increase of cardiac output per unit of time with increase in rate of contraction. With a rate beyond certain limits, however, the period of rapid filling is incroached on and the output falls. This is evident clinically in cases of paroxysmal tachycardia in which the rhythm is regular and each beat may be of an entirely normal character, but owing to the very rapid heart rate, the output per unit of time is decreased. The systolic arterial pressure falls and the venous pressure rises.[2] This change is also evident by the venous engorgement (cyanosis, liver enlargement, laryngeal edema, etc.) which may occur in prolonged attacks.

* From the Department of Physiology of the University of Wisconsin.

1. Henderson: Am. J. Physiol. **16**:325, 1906.
2. Hooker and Eyster: Bull. Johns Hopkins Hosp. **19**:274, 1908.

Of greater importance in their relation to cardiac disease in general, however, are those more severe and less transitory affections which involve not only the rate, but also the coordination of the beat, and which are usually, but not always, accompanied and preceded by valvular disease and more or less myocardial injury. These comprise extrasystoles, auricular flutter and fibrillation, partial heart block, and idioventricular rhythm in complete auriculoventricular dissociation. In partial dissociation, the reduction in ventricular efficiency is due merely to the slow ventricular rate. Auricular fibrillation is equivalent to auricular paralysis, so far as the pumping action of the auricles is concerned, and the decrease in pumping capacity of the ventricles is due, at least in part, to their increased rate.

Another factor seems to play a rôle in this case, however, namely, the prematurity of many of the ventricular beats, as will be discussed later in more detail. The other types involve disturbances in the coordination between auricular and ventricular contraction. The rôle that the auricular contractions play in the normal rhythm in filling the mammalian ventricle has been investigated by Henderson,[1] Straub[3] and Gesell.[4] The last mentioned investigator differentiated between the influence of the absence of auricular contraction and the influence of interference produced by auricular contractions occurring incoordinated with ventricular systoles. The methods were, first, abolition of auricular contractions by producing auricular fibrillation, and second, the influence of auricular systoles in their time relations to ventricular systole during experimental complete heart block with a ventricular rate maintained by rhythmic stimulation. The criterion used was mean arterial blood pressure. Gesell obtained changes in blood pressure amounting to 55 per cent. of the pressure in the absence of auricular contractions by gradually shifting the time relations of auricular contractions with respect to ventricular contractions. With an independent ventricular rate, abolition of the auricular contraction causes a reduction of arterial pressure amounting to from 10 to 15 per cent. It is, therefore, evident that disturbances in cardiac rhythm, involving absence or incoordination of the auriclar contractions, must involve a reduction in the pumping efficiency of the heart.

In recent years there has been much interest in abnormal cardiac rhythms. This interest has been mainly, however, in reference to their causes, diagnosis, prognosis and relation to other cardiac conditions. So far as we have been able to find, there has been only one study made as to their mechanical effect on the circulation, and this

3. Straub: J. Physiol. **11**:378, 1910.
4. Gesell: Am. J. Physiol. **29**:36, 1911.

only in reference to one type of abnormal rhythm. Lewis[5] studied the influence of auricular fibrillation on cardiac output, mean arterial pressure and venous pressure in cats and dogs. He found a decreased cardiac output, with usually a fall of arterial and rise of venous pressure, and ascribed the change entirely to the abnormal ventricular rate.

The experiments described in the present work were undertaken to determine under experimental conditions the influence on the pumping efficiency of the heart of the various types of abnormal cardiac rhythms that occur clinically. The abnormal rhythms studied were frequent ectopic beats, auricular flutter and fibrillation and partial and complete auriculoventricular dissociation.

METHODS

Dogs were used exclusively. The animals were etherized and the thorax opened under artificial respiration. The ventricular output was measured by means of a plethysmograph connected with a balanced piston recorder. Mean arterial pressure from the femoral artery was recorded by a mercury manometer. Ectopic beats (extrasystoles) were produced by induction shocks applied to the auricles and ventricles during early diastole at rhythmic intervals (after every fourth or eighth normal beat) by means of the stimulus selector described by Hirschfelder and Eyster.[6] Auricular flutter and fibrillation were induced by faradic stimulation of the right auricle, and auriculoventricular heart block was produced by heating the region of the auriculoventricular node and upper part of the bundle by a thermode applied through the right auricular appendage.

EXPERIMENTAL RESULTS

Extrasystoles.—So far as the mechanical efficiency of the heart is concerned, it is important to consider that an extrasystole is practically always a premature beat, or occurs at a shorter interval of time after the preceding normal beat than usual, and that it is followed by a compensatory pause. Owing to the fact that it is premature, with a reduced diastole period during which the ventricle receives its complement of blood, it is a more or less deficient beat as compared to the normal. With extrasystoles we have, therefore, the replacement of a certain number of normal cardiac systoles by less efficient contractions.

The influence of auricular extrasystoles every fourth, eighth and sixteenth beat on cardiac output and arterial pressure is summarized in Table 2. The average effect was somewhat greater the more frequent the extrasystoles, but in most cases was relatively small and in

5. Lewis: J. Exper. M. **16**:395, 1912.

certain individual cases probably within the normal variations of cardiac output. In several instances there was a slight increase above the normal, probably again within normal variations of output.

TABLE 1.—EXAMPLES OF TYPICAL EXPERIMENTS

Character of Rhythm	Auricular Rate	Ventricular Rate	Ventricular Output per Minute	Percentage Decrease	Mean Arterial Pressure	Percentage Decrease
Normal	168	168	2020.8	....	106	
Auricular fibrillation	...	180	798.48	79.6	68	35.2
Normal	168	168	2252.88	....	102	
Normal	186	186	1217.66	....	60	
Auricular flutter	348	174	926.50	24.9	49	18.0
Normal	180	180	1197.72	....	60	
Normal	138	138	1881.6	....	70	
Auriculoventricular heart beat 2:1	144	72	1144.08	39.2	44	37.1
Normal	132	132	2079.84	....	76	
Normal	138	138	1881.6	....	70	
Auriculoventricular heart beat complete	126	36	652.2	65.3	46	34.3

TABLE 2.—SUMMARY OF ALL EXPERIMENTS

Character of Rhythm	No. of Observations	Percentage Decrease in Cardiac Output		Percentage Fall in Blood Pressure	
		Average	Variations	Average	Variations
Extra systoles every 4th to 8th beat	8	6.9	+3.7 to —11.2	0	
Extra systoles every 10th beat	2	0	.....	0	
Auricular flutter	15	15.6	+8 to —34.9	15.2	+8 to —40
Auricular fibrillation	7	40.6	15.2 to 79.6	34.8	25 to 55
Auriculoventricular heart block, partial (2:1)	4	44.0	39.2 to 50	33.0	30 to 37.1
Auriculoventricular heart block, complete	13	60.6	58.4 to 65.3	39.4	35.3 to 52

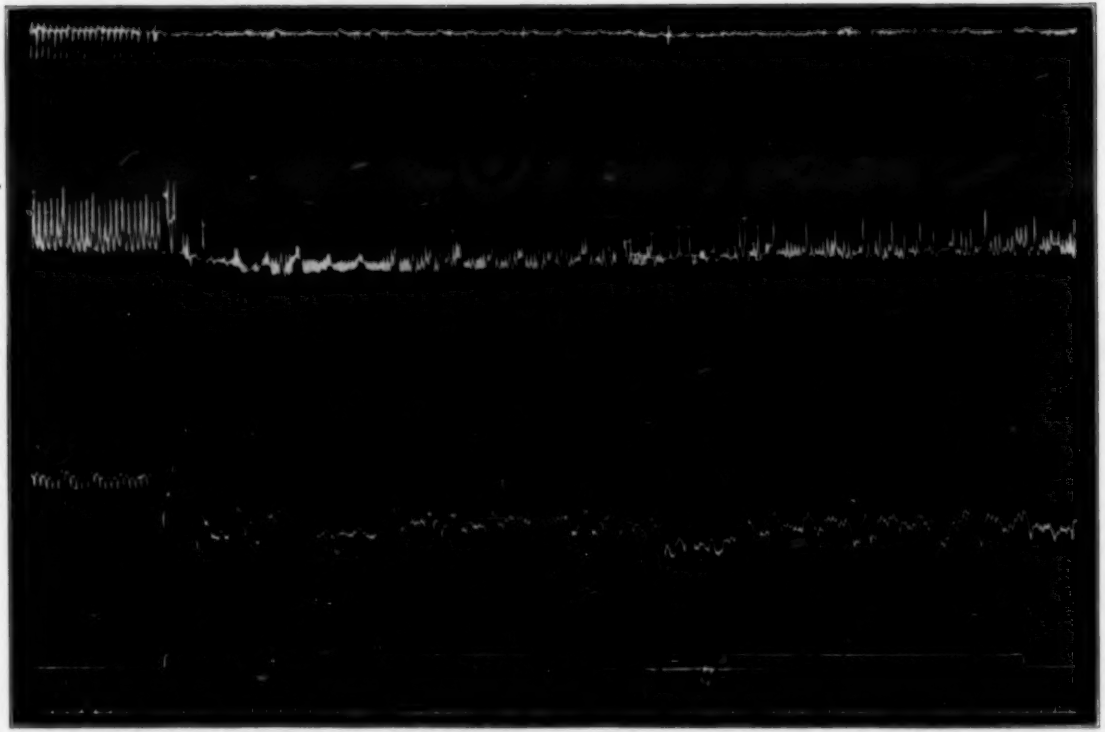
Theoretically, the degree of mechanical influence of extrasystoles would depend upon their number and on their prematurity. Furthermore, ventricular extrasystoles, because of the absence of or interference with auricular contraction and possibly because of atypical ventricular systoles, would be expected to produce a somewhat greater mechanical influence than an equal number of auricular extrasystoles. Attempts were made to obtain the same incidence of the extrasystoles in the different experiments, but we have not studied variation of incidence, nor have we combined ventricular with auricular extrasystoles.

Auricular Flutter and Fibrillation.—Stimulation of the right auricle by rapidly increasing induction shock leads, as is well known, to flutter or fibrillation of the auricle. The former type of rhythm is characterized by a very rapid but coordinated contraction of the auricle, in the latter coordinated auricular beats are replaced by incoordinated segmental contractions of different muscular bundles of the dilated auricle

and the condition is equivalent to auricular paralysis. In either case the ventricle follows the abnormal auricular rhythm in an irregular manner and shows both irregularity in rhythm and in size of contraction (totally irregular pulse or pulsus irregularis perpetuus). Aside from the rapid ventricular rate, many of the beats are quite premature in character, and these not infrequently occur in a series of several ventricular beats followed by pauses which may be even longer than normal cycles. Especially in auricular fibrillation, many of the ventricular beats are so premature that the intraventricular pressure does not rise sufficiently to open the semilunar valves, and from the pumping standpoint are therefore totally inefficient. Experimentally, one may secure auricular tachycardia, flutter and fibrillation in most experiments by successively increasing the rate of auricular stimulation. With a rate of stimulation less than 250 per minute, each auricular contraction is usually followed by a ventricular contraction in the usual manner. Increasing the rate of stimulation may lead to an auriculoventricular heart block with the auricles beating twice as fast as the ventricles, or more frequently the impulses are conducted irregularly to the ventricles and an irregular ventricular rhythm occurs. Increasing the rate, especially if also the strength of the stimulus is increased, leads usually to auricular fibrillation, with, as a rule, an increased irregularity of ventricular contractions.

The experimental results of auricular flutter on cardiac output show considerable variation in the different trials. In a few there was actual increase in output, but the majority showed a decrease, reaching a maximum of 34.9 per cent. of the normal, as shown in the accompanying illustration. In the former, the ventricular rates were usually, but not always, lower than when a decrease occurred. The factors that should be considered as entering into the production of a decreased ventricular output in auricular flutter are (1) the degree of increase of ventricular rate; (2) the proportion of premature ventricular beats, and (3) the interference effects produced on ventricular fillings by the auricular systoles. Variations in the operation of these different factors no doubt explain the difference in degree of decrease of output produced.

Auricular fibrillation consistently decreased cardiac output, and the effect was in most cases much greater than in auricular flutter. It is important to note that this was not the result of a more rapid ventricular rate in fibrillation than in flutter, and to explain the greater effect in the former we must assume a larger proportion of premature and abortive beats or ascribe an important difference in the influence that auricular tachysystole and auricular paralysis exert on ventricular filling. The larger proportion of abortive ventricular beats in auricular



Experimental auricular fibrillation. The top record records the contraction of the right auricle. The second record is made by a ventricular cardiometer, the downstroke representing systole. The third record is mean arterial blood pressure from the femoral artery. The fourth and fifth records are those of the signal pen and time marker (one second intervals), respectively. During the period marked by the signal pen, auricular fibrillation was induced by faradic stimulation of the right auricular appendage. The record is to be read from left to right.

fibrillation is usually very evident on inspection of the tracings, but why impulse conduction to the ventricle in auricular fibrillation should be more irregular than in auricular flutter is not entirely clear.

There are probably at least three factors acting in auricular flutter and fibrillation to decrease ventricular output: (1) an increase in ventricular rate beyond the optimum; (2) the presence of a variable number of premature and abortive beats, and (3) auricular interference or paralysis. That the first factor is not the sole one is shown by the fact that the decrease in output is not proportionate to the increase in ventricular rate.

Study of the tracings would seem to indicate that the main factor is ventricular irregularity and the presence of abortive and premature ventricular systoles. Auricular fibrillation is characterized particularly by the large proportion of inefficient ventricular beats (pulse deficiency). The third factor, auricular interference in flutter and auricular paralysis in fibrillation, must also play a considerable rôle. This influence is exerted on ventricular filling and probably has a different proportionate influence with different ventricular rates. A more rapid auricular rate in flutter would presumably tend to increase the probability of interference.

Auricular Ventricular Heartblock. — In partial heartblock, the decrease in mechanical efficiency is due entirely to the slow ventricular rate. In complete block, an additional factor has to be considered, namely, the absence of the normal influence of the auricular contraction on ventricular filling. Some of the auricular contractions must be so placed as to actually produce interference with filling. Due to the slow ventricular rate in each case, it is found, however, that the filling is probably more complete than normal, since the output per beat is actually greater than in normal rhythm. The decrease in minute volume output is, therefore, due to the slow rate of contraction of the ventricle. In both partial and complete auriculoventricular block the reduction in volume output was approximately proportional to the percentage reduction in the ventricular rate. The effect was greater in partial block and the former shows the greatest average reduction of any of the abnormal types of cardiac rhythm.

Changes in Mean Arterial Pressure.—With a moderate degree of decrease in output, there is an approximately proportionate fall in mean blood pressure. When the output is markedly decreased, as in auricular fibrillation and heartblock, the fall in pressure is frequently considerably less than the decrease in output, indicating the occurrence of compensatory factors.

CONCLUSIONS

1. Frequent extrasystoles (occurring every fourth to eighth cycle) occurring in an otherwise normal cardiac rhythm have little influence in reducing the mechanical efficiency of the heart.

2. Auricular flutter and fibrillation produce a variable reduction in the volume output of blood from the ventricles, depending on the degree of development of the abnormal rhythm. The effect in fibrillatiion is greater than in flutter, and is mainly due to the irregularity of the ventricle and to the high percentage of premature and abortive ventricular beats, rather than to the fast ventricular rate.

3. Partial and complete auriculoventricular dissociation produce a marked reduction in ventricular output, due to the abnormally slow ventricular rate. In complete dissociation the reduction in mechanical efficiency is usually greater than in any other type of abnormal rhythm.

4. The mean arterial pressure tends to fall as the ventricular output is reduced, but not to the same degree as the output when this is much affected, indicating the occurrence of compensating factors tending to maintain an approximately normal arterial pressure.

ON THE PLATELET COUNT AND BLEEDING TIME IN DISEASES OF THE BLOOD*

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The blood platelets, the third corpuscular element of the blood, have since the fundamental work of Bizzozero, been the object of many researches, the results of which, in brief, are the following:

1. The platelets are a normal element of the blood of great importance for coagulation and thrombosis.

2. The place of origin of these bodies is not known with absolute certainty, although most authors believe in Wright's theory, that traces their descent to the megakaryocytes of the bone marrow.

3. The platelet count normally varies more than does the number of red and white cells.

4. The platelet count is low in genuine, idiopathic purpura, and in certain diseases of the blood and infections (pernicious anemia and typhoid).

5. When the number of platelets falls below certain values, the symptoms of a hemorrhagic diathesis occur.

The methods for counting the platelets hitherto published, all use blood from a skin prick and may be divided in two groups:

1. Direct count in dilutions after the ordinary hemocytometric principle, but using special liquids (Hayem, Afanassiew, Wright, Kinnicutt, etc.).

2. Indirect count, in which the relation of platelets to erythrocytes is counted in a variable dilution with a fixing liquid, thus avoiding the use of pipettes (Kemp, Brodie and Russell, Pratt, Fonio, etc.).

Different authors have estimated the normal platelet count as between 200,000 and 800,000 per c.mm., all, however, agreeing that the boundary lines of the normal must be placed rather widely apart.

In 1918, Oluf Thomsen[1] introduced a new technic for the enumeration of the platelets, which makes this procedure infinitely more reliable than previously.

The technic, in brief, is as follows:[2]

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* From the medical clinic of the Copenhagen University; Prof. Knud Faber.

1. Hospitalstid. **62**:161 (Feb. 5) 1919.

2. The procedure described is slightly modified from the original method of Thomsen.

In a 5 c.c. centrifuge tube, graduated in one-tenth c.c., measure 0.5 c.c. of a 10 per cent. sodium citrate solution. By venepuncture with a sharp, not too narrow, needle 4.5 c.c. of blood are run down into the citrate solution and mixed with it by corking and shaking. The blood adhering to the cork is wiped off with a piece of cloth or filter paper, and the tube is left to stand for about an hour.

In all cases, except severe polycythemia, the red blood cells, and most of the white blood cells, have been precipitated so as to leave a layer of turbid plasma *containing the platelets in a homogeneous and very stable suspension,* which does not undergo any change for at least five hours. A small quantitiy of this mixture is drawn off with an ordinary white blood cell melangeur, and diluted in the proportion of 1:20 with a solution containing 9 $^{0}/_{00}$ sodium chlorid and 2 $^{0}/_{00}$ liquor formaldehydi, possibly also a small quantity of brilliant cresyl blue to stain the platelets.

The technic of Ellermann and Erlandsen, necessitating the use of separate pipettes for "blood" and diluting fluid, is to be recommended (*Ugesk. f. laeger,* No. 6, 1912).

A drop of the plasma dilution is placed in the ordinary closed counting cell of Thoma (Bürker's and other open models must not be used on account of the evaporation).

In the dilution, the platelets sediment readily, and may be counted after standing from one-half to one hour. The platelets show as small refractive bodies of a blue color at low focus.

By counting ten large squares and dividing the total with two, the number of platelets in thousands contained in 1 c.mm. of citrated plasma is found.

When the relation of citrated blood and the volume of the blood cells are known, the platelet count per c.mm. of blood may easily be calculated.

According to Oluf Thomsen, the precipitate, on centrifuging the blood for ten minutes at 2,000 revolutions per minute, still contains 5 per cent. of plasma. This value I have found a little low, since centrifuging for fifteen minutes, at 3,000 revolution per minute, still leaves from 5 to 10 per cent. of plasma among the cells.

In the determinations that I have carried out, the precipitate after one and one-half hour of centrifuging, which conforms very nearly with the hematocrit results, have been used as a measure for the bulk of the blood cells.

The calculation of the platelet count is then made from the following formula or by multiplying with a constant calculated for each value of the precipitate:

$$\text{Platelet count} = \frac{(\text{citrated blood} \div \text{precipitate}) \times \text{platelets per c.mm. plasma}}{\text{Citrated blood} \div \text{citrate}}$$

The error caused by an inaccurate determination of the cell volume is not large, as is shown by the following example:

Citrated blood = $\frac{0.5}{4.5}$ (a) precipitate after 15 minutes' centrifuging 2 c.c.
(b) precipitate after 1½ hours' centrifuging 1.8 c.c.[3]

Counted 500,000 platelets per c.mm. citrated plasma

Platelet count calculated by (a) 333,000 per c.mm.
(b) 355,000 per c.mm.

The results of counts in double specimens and in the same plasma after varying times have convinced me of the reliability of the method. Within five hours from the taking of the blood there is no loss of platelets from sedimentation. In clean punctures, with good needles, the platelets never adhere to the other blood cells. Small bore needles, such as are used for hypodermic syringes, cause agglutination of the platelets, therefore, must never be used. The few leukocytes found in the counting cell must not show adhering platelets.

The research that I have carried out was made on mixed material, consisting of hospital patients in the wards of the Rigshospital and other Copenhagen hospitals.

Consequently, the difficulties in drawing the boundary lines of the normal may be somewhat greater, but the conclusions seem to me to be more valuable than those to be drawn from an examination of a necessarily smaller number of absolutely normal persons. In 122 individuals, with seemingly indifferent diseases, 179 examinations were made, and the platelet count varied between 200,000 and 500,000 per c.mm. of blood.

If we arrange these results in groups of 50,000 we find the following:

TABLE 1.—Normal Platelet Counts

Platelet Count	Number of Examinations	Number of Persons
200,000–250,000	21	10
251,000–300,000	22	16
301,000–350,000	36	34
351,000–400,000	48	38
401,000–450,000	27	33
451,000–500,000	13	10
Total	179	122

The majority of the determinations show platelet counts between 300,000 and 450,000 per c.mm.

Before giving the results of the platelet count in cases of blood disease, I would mention the fact that a slightly diminished number of platelets was found in one case of acromegaly, but not in two other

3. Red cells, 5; 62,000,000 per c.mm.

cases, and in one case of typhoid fever (third week), but not in two other cases (first and second week, respectively). Counts above 500,000 were found irregularly in the course of some acute infections.

In accordance with other observers I found the platelet count normal in two cases of hereditary hemophilia and slightly elevated in a third case, showing a pronounced simple anemia.

In one case of hemolytic icterus with blood alterations of the pernicious type, the plate count showed very low normal values, once even less than 200,000.

TABLE 2.—Hemophilia

Number	Date	Platelets	Hemoglobin per Cent.	Red Blood Cells, Millions	Color Index	White Blood Cells	Bleeding Time, Minutes
1	4/23	402,000	87	5.14	0.84	6,100	2
	5/27	457,000	91	5.19	0.88	7,200	3
2	5/27	394,000	93	5.24	0.89	6,400	8
3	6/26	528,000	69	4.65	0.86	9,100	
4	1918	.....	..	....	....	.....	3

TABLE 3.—Icterus Hemolyticus

Number	Date	Platelets	Hemoglobin per Cent.	Red Blood Cells, Millions	Color Index	White Blood Cells	Bleeding Time, Minutes
1	5/31	213,000	44	1.99	1.11	6,200	3
	6/ 6	216,000					
	6/12,	220,000	50	2.08	1.22	4,500	
	6/30	186,000	48	2.30	1.02	4,800	6

As simple anemias I have classed those cases in which the hemoglobin percentage was less than 70 (100 per cent. hemoglobin = 18.5 per cent. oxygen capacity), in which the colorimetric index was less than 1, and in which there were no signs of any other disease of the blood.

In twenty-one such patients (six cases of cancer, seven of anemia due to hemorrhage, and eleven obscure simple anemias) I have carried out twenty-seven platelet enumerations.

Thirteen determinations made in eleven patients were normal, rather high values, while fourteen determinations on ten patients showed increased counts. The platelet counts observed in some cases were over 1 million per c.mm.

No constant relation between the platelet count and the cause or degree of the anemia could be traced, but, possibly, the result may be of some prognostic value, a high platelet-count indicating a better regenerative power of the bone marrow.

The results in pernicious and pernicious aplastic anemia are shown in Table 4.

Of the sixteen cases tabulated, fourteen were typical genuine pernicious anemia, while two (numbers 8 and 9) belonged to a more aplastic type. As the latter both died and the postmortem confirmed the diagnosis, I feel safe in ranging them in here.

TABLE 4.—PERNICIOUS ANEMIA

Number	Date	Platelets	Hemoglobin per Cent.	Red Blood Cells, Millions	Color Index	Bleeding Time, Minutes
1	12/29	144,000				
	1/ 9	107,000	76	3.90	1.18	
	1/24	128,000				
	2/15	140,000	67	3.80	1.01	
	3/15	161,000	..	....	....	5½
2	3/ 6	66,000	..	....	....	10
	3/11	61,000	..	....	....	9½
	3/21	74,000	..	....	....	9
	4/ 1	55,000				
	4/24	83,000	46	1.51	1.51	7
	5/14	95,000	47	....	....	5
	6/14	74,000	49	1.58	1.55	>10
	7/ 1+	87,000	32	1.19	1.34	>10
3	4/29	188,000	79	3.80	1.04	
4	5/24+	36,000	16(?)	0.86	....	>10
5	5/31	116,000	82	1.87	1.40	2½
	6/ 7	108,000	80	1.65	1.56	5
	6/14	90,000	86	1.90	1.47	
	6/21	173,000	63	2.02	1.56	
	6/28	177,000	73	2.40	1.49	3
	7/ 7	268,000	82	2.63	1.56	2½
6	7/ 4	116,000	45	1.45	1.55	
7	7/ 4+	16,000	15	0.71	1.06	>10
8	5/ 2+	34,000	14	0.61	1.15	>10
9	2/20	105,000	47	1.96	1.23	3½
	2/25+	40,000	35	1.43	1.22	7½
10	8/16	110,000	25	0.71	1.76	5
11	8/25	198,000	56	2.14	1.31	
	10/ 9	451,000	91	3.91	1.16	
12	8/30	246,000	45	1.80	1.19	3½
13	9/ 6	55,000	43	1.53	1.40	
	9/19	22,000	28	0.93	1.51	>10
14	9/29	56,000	31	0.95	1.63	>10
15	10/27	22,000	28	1.05	1.3	
	11/ 1	25,000	27	0.96	1.4	
16	10/22	13,000	21	0.57	1.8	
	10/30	16,000	16	0.42	1.9	

Evidently, in pernicious anemia one generally finds a diminished platelet count, most pronounced in the grave cases (Cases 2, 4, 7, 8, 9, 13, 14, 15 and 16), less so in the milder cases and during remissions.

In two cases, when the hemoglobin and red blood cell values reached nearly the normal (Cases 5 and 11), the platelet count also became normal. In Case 12 there was a low normal platelet count, but this patient, whom I have not had the opportunity of studying further, was convalescing rapidly and was soon discharged.

The value of the study of the platelets in pernicious anemia rests on their importance for the differential diagnosis between simple anemias and those of Biermer's type, and furthermore on their value as a means of making a prognosis.

Cases in which the platelet count has gone very much under 100,000 per c.mm. generally terminate fatally, while those with higher counts tend to remissions.

Complications in diagnosis might arise in cases of simple anemia following genuine purpura, but this disease seems to be very rare in Denmark, since I have only observed one case in a child and that before beginning this series of observations.

In leukemia the behavior of the platelets is more variable (Tables 5 and 6).

TABLE 5.—Myeloid Leukemia

Number	Date	Platelets	Hemoglobin per Cent.	Red Blood Cells, Millions	Color Index	White Blood Cells	Bleeding Time, Minutes
1	2/10	83,000	47	2.39	0.96	249,000	>10
	2/17	96,000	..	....	....	.....	>10
	2/24	75,000	..	....	....	100,000	
	3/ 5	118,000					
	3/12	134,000	..	....	....	107,500	>10
2	5/30	362,000	26	1.15	1.12	40,100	2½
	6/ 6	302,000	21	1.04	1.00	32,600	3½
	6/16	247,000	19	0.85	1.03	19,700	3
3	4/23	771,000	70	4.30	0.81	181,700	2
	5/ 6	568,000	52	2.91	0.89	27,000	2
4	4/ 1	1,366,000	85	4.81	0.98	75,000	3
	4/ 7	1,291,000	..	....	....	66,200	2
5	9/24	405,000	58	4.20	0.70	22,500	

TABLE 6.—Lymphatic Leukemia

Number	Date	Platelets	Hemoglobin per Cent.	Red Blood Cells, Millions	Color Index	White Blood Cells	Bleeding Time, Minutes
1	12/30	173,000	82	3.94	1.05	15,600	
	1/16	127,000	90	4.10	1.09	6,000	5½
2	4/20	86,000	72	3.80	0.95	94,000	4
3	4/21	134,000	85	1.30	1.35	120,000	5½
4	3/29	170,000	78	4.35	1.15	247,000	2½
	4/ 7	175,000	..	....	....	.....	2
	4/22	156,000	..	....	....	.....	2
	5/ 5	127,000	73	3.90	0.94	106,000	3
	5/15	146,000	79	4.02	0.98	144,000	2
	6/ 2	122,000	78	3.88	1.00	125,000	2½
	6/21	139,000	66	2.60	0.92	63,100	
5	6/16	296,000	90	5.56	0.79	92,500	3
	6/17	287,000					
	7/ 2	314,000	97	5.42	0.89	108,400	4
6	4/22	48,000	59	3.10	0.95	2,200	
	4/29	48,000	..	....	....	.....	>10
	5/13	36,000	56	3.07	0.91	2,400	
	5/28	49,000	51	2.66	0.96	3,200	>10
	6/17	58,000	60	3.11	0.96	1,800	
7	8/17	7,000	14	0.67	1.04	166,000	>10

In seven cases of lymphatic leukemia, the platelet count was low in six, but slightly so in three cases, considerably lower in the remaining three cases, one of which must be set apart on account of its showing at the time of the examination, a blood picture more like an aplastic anemia (Case 6).

In myeloid leukemia the results were even more divergent, inasmuch as one case showed a very low platelet count, two had normal values and two had a very considerable increase. It may be of importance to remark that the two first cases showed blood alterations resembling those of pernicious anemia.

Inasmuch as these variations are inconstant, one cannot attribute any diagnostic value to them, and the platelet count in leukemia only serves to direct our attention to an impending hemorrhagic diathesis.

The reason for the low counts in leukemia is obscure. It cannot be explained by the roentgen-ray treatment used, as three of the six patients with lowered platelet count never had been treated before, and two of the five patients with normal or increased values had been treated previously; also, the platelet count showed no drop during an effective roentgen-ray treatment.

In many of the cases mentioned the platelet count was low without any signs of hemorrhagic diathesis appearing. In order to bring a latent tendency to hemorrhage to light, I have carried out a large number of bleeding time determinations by Duke's method. The blood from a small skin prick (2 mm. deep) was wiped off every one-thirtieth second till the bleeding stopped. I found the normal bleeding time in about 100 determinations to lie between one and one-half and four minutes.

In Tables 1 to 6 the bleeding time is found on the extreme right.

In the only case of hemolytic icterus examined (Table 2) the bleeding time at first was normal, but became slightly lengthened, when the platelet count dropped to 186,000 per c.mm.

From Tables 4, 5 and 6 it appears that the bleeding time may be moderately prolonged when the number of platelets lies between 100,000 and 200,000, e. g., in pernicious anemia (Case 1), where a platelet count of 181,000 occurred, together with a bleeding time of five and one-half minutes. The lower the number of platelets falls, the more likely one is to find a definitely long bleeding time. In a single case (lymphatic leukemia, Case 2) the bleeding time was normal (four minutes), although the platelet count was 86,000.

In all other cases where the platelet count fell below 100,000 per c.mm., one finds a protracted bleeding time, often longer than ten minutes.

In three out of four cases of hemophilia with a normal platelet count, the bleeding time also does not exceed the average limits. In a fourth case it is somewhat lengthened. In all cases of simple anemia the bleeding time was normal, even rather shorter than normal.

SUMMARY

1. The method of Oluf Thomsen for counting the platelets in citrated plasma is described.

It gives reliable results. At the same time it permits a determination of the prothrombin time with a slight alteration of the technic of Howell, also a determination of the fibrin percentage according to an unpublished method elaborated by the author, thus making possible a systematic examination for hemorrhagic diathesis on a single blood specimen.

2. The number of platelets in normal individuals lies between 200,000 and 500,000.[4]

3. The platelets are diminished in number in pernicious anemia, in most cases of lymphatic leukemia and in some cases of myeloid leukemia. Normal values are found in hemophilia, and augmented values are found in many cases of simple anemia and some of myeloid leukemia.

4. The diagnostic and prognostic importance of the platelet count in diseases of the blood is discussed.

5. The bleeding time determination of Duke helps to disclose a latent hemorrhagic diathesis due to platelet deficiency, as symptoms may not appear without a provocative cause. It is shown that platelet counts of less than 100,000 per c.mm. generally cause a tendency to bleed.

6. The counting of the platelets and determination of the bleeding time is of extreme importance as a pre-operative measure, especially in cases of aplastic anemia, in which an operation often is performed for explorative purposes, occult cancer being suspected.

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4. In absolutely normal persons the number of platelets rarely is less than 300,000 per c.mm.

Book Review

TOTAL DIETARY REGULATION IN THE TREATMENT OF DIABETES. By Frederick M. Allen, M.D., Edgar Stillman, M.D., and Reginald Fitz, M.D. Monographs of the Rockefeller Institute for Medical Research, No. 11, Oct. 15, 1919. The Rockefeller Institute for Medical Research, New York.

The monograph opens with a history of diabetes written from the standpoint of treatment which, with bibliography, fills seventy-eight pages. It is stated in the preface that it was written as the opening chapter of a treatise in three parts, and that it was to have been followed by chapters which do not appear in the present volume. The latter, according to the original plan, would have been published in a separate section. The history is followed by a detailed exposition of the management of diabetic patients as carried out in the Rockefeller Institute. Following this there are 284 closely printed pages and numerous charts devoted to the clinical records in full of seventy-five cases of diabetes treated at the same institution. The remainder of the volume contains chapters on phases of the problem which Allen and his co-workers have made the subject of special investigation, thus: a chapter on pancreas feeding; a chapter on exercise, and one on the influence of fat in the diet. These are followed by a discussion of results and prognosis, and a chapter on etiology and pathology.

One familiar with the literature of diabetes, including especially the previously publishd works of Allen and Joslin, will find in the volume little that is strictly new. The detailed case records have not been published before, and they form an important feature, but apart from these, the work is largely a restatement of the work and views of Allen and his co-workers.

The historical part indicates that previous writers had established the principle of making the diabetic patient sugar-free and of keeping him consistently sugar-free thereafter, whenever this was possible. It had been accomplished in cases sufficiently mild by restricting the carbohydrate alone. In a less mild group of cases it had been accomplished by restricting the protein as well as the carbohydrate. It was known that even in the most severe cases fasting, sufficiently prolonged, would result in the disappearance of all symptoms of diabetes, provided there were no preventing intercurrent disease. It was not realized that the severest cases, or even the moderately severe cases, could be kept consistently free of symptoms of diabetes for an indefinite period of time after they were desugarized by fasting. Fear of the effects of continued undernutrition of the degree and kind thought necessary had led to the practice of increasing the diet too rapidly and too much, so that symptoms promptly returned. Allen desugarized all, or nearly all, patients by an introductory fast and subsequently refrained from adding food beyond the limits of the patient's power to assimilate it. He thus extended the principle of desugarizing and keeping the patient consistently sugar free to a large group of cases for whom this had not been considered feasible. In so doing he discovered new possibilities in the line of restoration of tolerance and the conversion of the more severe into the less severe or milder types of diabetes. The gradual addition of measured quantities of carbohydrate, protein and fat to desugarized diabetic patients who proclaim the limit of their assimilative powers by excreting abnormal quantities of sugar or acid proved a good method for studying the

metabolic effects of the foodstuffs individually and collectively. This method, applied with the facilities of the Rockefeller Institute, has led to a much clearer concept of the principles underlying the dietetic management of diabetes than had been held before. Total dietary regulation and the deleterious effects of an undue quantity of fat in the diet are emphasized throughout the work.

The book is written somewhat in the form of a diary, in that views and cases are presented in their entirety in the order of their arrival. It contains much valuable data which would be more easily accessible if it were classified, indexed and separated from the nonessential, but it tells the story of an advance in the dietetic management of diabetes that has resulted in a decrease of suffering and a prolongation of life. It is a work which should be read by all those who assume responsibility for the care of diabetic patients.

Fifty cents each will be paid for the following issues of the Archives of Internal Medicine: January, March, June, August, 1918. January and July, 1916; November, 1915; January, 1911; July, 1909. AMERICAN MEDICAL ASSOCIATION, 535 North Dearborn Street, Chicago, Ill.